IX. Appendices

Guideline for Prevention and Control of Norovirus Gastroenteritis Outbreaks in Healthcare Settings

APPENDIX TABLE OF CONTENTS

APPENDIX 1A: SEARCH STRATEGY FOR GUIDELINES

Database	Platform
National Guideline Clearinghouse	http://www.guideline.gov/
MEDLINE	OVID
EMBASE	OVID
Cochrane Library	Wiley Interscience
NIH Consensus Development Program	http://consensus.nih.gov/
National Institute for Health and Clinical Excellence	http://www.nice.org.uk/
Scottish Intercollegiate Guidelines Network	http://www.sign.ac.uk/
USPSTF	http://www.ahrq.gov/clinic/uspstfix.htm

NATIONAL GUIDELINE CLEARINGHOUSE

Keyword	Search Results
norovirus	2
Norwalk	6
“viral gastroenteritis”	6

MEDLINE

#	Search History	Results
1	exp norovirus/	1196
2	(norwalk or norovirus).mp.	1680
3	small round structured virus$.mp.	192
4	exp Virus Diseases/ and exp Gastroenteritis/	6314
5	((virus$ or viral) adj10 gastroenteritis).mp.	2121
6	or/1-5	8414
7	limit 6 to (guideline or practice guideline)	13

EMBASE

#	Search History	Results
1	exp norovirus/	516
2	(norwalk or norovirus).mp.	1494
3	exp Small Round Structured Virus/	33
4	((virus$ or viral) adj10 gastroenteritis).mp.	2884

5	exp Viral Gastroenteritis/	142
6	or/1-5	3383
7	exp Practice Guideline/	127276
8	6 and 7	42

COCHRANE LIBRARY

#	Search History	Results
#1	MeSH descriptor norovirus, this term only	3
#2	norovirus OR Norwalk	54
#3	(#1 OR #2) *Restricted to Technology Assessments*	0

NIH Consensus Development Program

No relevant guidelines were found

National Institute for Health and Clinical Excellence

Keyword	Search Results
norovirus	0
Norwalk	0
gastroenteritis	0

Scottish Intercollegiate Guidelines Network

No relevant guidelines were found

USPSTF

No relevant guidelines were found

***25 relevant guidelines identified*[25-48,49]**

APPENDIX 1B: SEARCH STRATEGY FOR SYSTEMATIC REVIEWS/PRIMARY LITERATURE

Database	Number of Hits*
MEDLINE (1950 to 2008 Week 5)	2324
EMBASE (1980 to 2008 Week 5)	1533
CINAHL (1987 to 2007 Dec Week 1)	160
Global Health (1910 to Dec 2007)	1064
Cochrane Library	33
ISI Web of Science	1463
Total (after removing duplicates)	**3702**

* On 02/07/2008

MEDLINE

#	Searches	Results
PHASE 1: SEARCH TERMS FOR NOROVIRUS		
1	exp norovirus/	1257
2	(norovirus$ or norwalk).mp. [mp=title, original title, abstract, name of substance word, subject heading word]	1773
3	(small round structured virus$ or SRSV).mp. [mp=title, original title, abstract, name of substance word, subject heading word]	205
4	norwalk-like virus$.mp.	353
5	winter vomiting disease.mp.	20
PHASE 2: SEARCH TERMS FOR CALICIVIRUS AND RESTRICTED VIRAL GASTROENTERITIS TERMS		
6	exp Caliciviridae/ or exp Calicivirus, Feline/ or calicivirus.mp. or exp Caliciviridae Infections/	2421
7	exp virus diseases/ and exp gastroenteritis/ and (exp disease outbreaks/ or outbreak$.mp. or exp horizontal disease transmission/ or exp health facilities/)	1112
8	(virus or viral).mp. and exp gastroenteritis/ and (exp disease outbreaks/ or outbreak$.mp. or exp horizontal disease transmission/ or exp health facilities/)	900

9	((virus or viral) adj5 gastroenterit$).mp. and (exp disease outbreaks/ or outbreak$.mp. or exp horizontal disease transmission/ or exp health facilities/)	297
10	(nosocomial adj5 gastroenteritis).mp.	53
11	(epidemic adj5 gastroenteritis).mp.	200
12	(non?bacterial adj5 gastroenteritis).mp.	145
13	exp virus diseases/ and exp diarrhea/ and (exp disease outbreaks/ or outbreak$.mp. or exp horizontal disease transmission/ or exp health facilities/)	491
14	(virus or viral).mp. and exp diarrhea/ and (exp disease outbreaks/ or outbreak$.mp. or exp horizontal disease transmission/ or exp health facilities/)	351
15	((virus or viral) adj5 diarrhea).mp. and (exp disease outbreaks/ or outbreak$.mp. or exp horizontal disease transmission/ or exp health facilities/)	217
PHASE 3: COMBINING PHASES AND APPLYING LIMITS		
16	or/1-15	4160
17	(addresses or bibliography or biography or clinical conference or comment or congresses or consensus development conference or consensus development conference nih or dictionary or directory or duplicate publication or editorial or festschrift or historial article or interview or lectures or legal cases or news or newspaper article or patient education handout).pt.	853201
18	16 not 17	4067
19	limit 18 to (humans and english language)	2324

EMBASE

#	Searches	Results
1	exp NOROVIRUS/	588
2	exp Norwalk Gastroenteritis Virus/	745
3	(norovirus$ or norwalk).mp.	1588
4	exp Small Round Structured Virus/	33
5	(small round structured virus$ or SRSV).mp.	161
6	norwalk-like virus$.mp.	309

7	winter vomiting disease.mp.	8
8	exp CALICIVIRUS/	2578
9	exp Viral Gastroenteritis/	188
10	or/1-9	3002
11	(book or conference paper or editorial or note or proceeding).pt.	1019316
12	10 not 11	2735
13	limit 12 to (human and english language)	1533

CINAHL

#	Searches	Results
1	(norovirus$ or norwalk).mp.	152
2	(small round structured virus$ or SRSV).mp.	14
3	norwalk-like virus$.mp.	42
4	winter vomiting disease.mp.	1
5	calicivirus.mp.	21
6	or/1-5	162
7	limit 6 to english	160

GLOBAL HEALTH

#	Searches	Results
1	exp norovirus/	929
2	(norovirus$ or norwalk).mp.	1112
3	(small round structured virus$ or SRSV).mp.	299
4	norwalk-like virus$.mp.	303

5	winter vomiting disease.mp.	547
6	or/1-5	1360
7	limit 6 to english language	1064

COCHRANE LIBRARY

#	Searches	Results
#1	MeSH descriptor norovirus explode all trees	10
#2	MeSH descriptor Norwalk virus explode all trees	5
#3	(norovirus*): ti,ab,kw OR (norwalk): ti,ab,kw	33
#4	(small round structured virus*): ti,ab,kw OR (SRSV): ti,ab,kw	0
#5	(norwalk-like virus*): ti,ab,kw	6
#6	(winter vomiting disease): ti,ab,kw	1
#7	#1 OR #2 OR #3 OR #4 OR #5 OR #6	33

ISI WEB OF SCIENCE

Searches	Results
Topic=(norovirus) OR Topic=(norwalk) OR Topic=(small round structured virus) OR Topic=(norwalk-like virus) OR Topic=(winter vomiting disease) Timespan=All Years. Databases=SCI-EXPANDED, SSCI, A&HCI. Refined by: Document Type=(ARTICLE OR REVIEW) & Languages=(ENGLISH)	1463

APPENDIX 2: EVIDENCE, GRADE AND STUDY QUALITY ASSESSMENT TABLES

Q1: What person, virus or environmental characteristics increase or decrease the risk of norovirus infection in healthcare settings?

EVIDENCE TABLE Q1

Person characteristics

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
Demographic characteristics						
MMWR; 2008 [79]	Prospective controlled study. 1,3,4	To investigate an outbreak at an elementary school.	Students and staff at an elementary school in Washington DC in February 2007. Students – median age 8 years (range 3-12 years); 55% female. Staff – median age 41 years (range 13-66 years); 92% female. 266 – 207 students and 59 staff.	**Symptomatic norovirus infection** *Bivariate analysis: All results RR (95% CI); p value* Being a student – 0.94 (0.66-1.34); 0.76 Being female – 1.13 (0.82-1.56); 0.52 Having an ill contact – 1.76 (1.16-2.67); 0.01 Classroom J (first) – 1.94 (1.34-2.80); 0.02 Library use: 0.94 (0.58-1.52); 0.87 Library computer use: 1.08 (0.41-2.84); 1.00 **Interventions implemented** District of Columbia Department of Health recommended -more thorough handwashing - cleaning all shared environmental surfaces with a diluted (1:50 concentration) household bleach -cleaning computer equipment (i.e., mice and keyboards) -excluding ill persons from school for at least 72 hours after resolution of illness	A case of gastrointestinal illness was defined as illness in a student or staff member with nausea, vomiting, or diarrhea, who was at the school February 2-18, 2007. Power and sample size not reported.	017_IL
Mattner, F; 2006 [57]	Prospective controlled study 1,3,4,6,7	To characterize risk factors for the clinical complications of norovirus infections (e.g. vomiting, diarrhea, potassium decrease, creatinine increase, C-reactive protein	All individuals working in or admitted to five wards (psychiatry, nephrology, gastroenterology, cardiology and trauma) at a university hospital in Germany in the period from the onset of clinical	**Clinical features in patients** (study duration 3 months) Diarrhea – 79/84; 95% Vomiting – 57/84; 68% Somnolence – 2/84; 2% Serum creatinine increase > 10% – 22/84; 26% Serum potassium decrease > 20% – 7/84; 8% **Comparisons of attack rates in patients and nurses** (study duration 3	Diarrhea was defined as three or more episodes of loose stools in a 24 hr period. Cases were considered to be norovirus-positive if samples from at least two	358_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
		increase)	symptoms of the first patient until 2 days after the last patient became symptom free. All patients and staff members who were affected with a sudden onset of diarrhea and/or vomiting were included as cases. Patients admitted with clinical signs were regarded as index cases, and patients admitted ≥48 hrs before developing clinical signs were regarded as nosocomial cases. 84 patients (72 acquired infection nosocomially) and 79 staff members (60 nurses). 3 norovirus positive patients were excluded from risk factor analysis. N for risk factor analyses was 53 for all outcomes except C reactive protein increase (N=52)	months) *All results are attack rate (%) in patients vs. nurses; P value* Psychaitry ward – 78 vs. 88; <0.01 Nephrology ward – 32% in the first period and 33% in the second period in patients. Data for nurses not given Gastroenterology – 27 vs. 90; <0.01 Cardiology – 42 vs. 44; 0.87 Trauma – 35 vs. 83; <0.01 Total – 38 vs. 76; <0.01 **Risk factors for complications of norovirus** (study duration 3 months) *VOMITING>1 DAY:* *Univariate analysis: All results OR; P value* Age > 65 years – 1.84; 0.30 Male gender – 0.91; 1.00 Underlying cardiovascular disorders – 2.7; 0.13 Underlying gastrointestinal disorders – 0.34; 0.31 Underlying autoimmune disease – 0.81; 1.00 Underlying renal disorders – 0.95; 1.00 Renal transplant – 1.31; 0.75 Underlying malignancy – P value 0.18; OR not reported Underlying trauma – 1.14; 1.00 Immunosuppressive therapy – 0.92; 1.00 Community acquired norovirus – 2.36; 0.19 *Multivariate analysis: All results OR (95% CI)* Underlying cardiovascular disorders – 7.17(1.59-51.2) Community acquired norovirus – 5.54(1.04-42.8) *DIARRHEA>2 DAYS:* *Univariate analysis: All results OR; P value* Age > 65 years – 3.58; 0.01 Male gender – 2.15; 0.12 Underlying cardiovascular disorders – 2.80; 0.15 Underlying gastrointestinal disorders – 0.22; 0.03 Underlying autoimmune disease – 4.67; 0.24 Underlying renal disorders – 1.77; 0.39 Renal transplant – 1.71; 0.54 Underlying malignancy – 0.07; 0.01 Underlying trauma – 0.27; 0.053	patients from the same ward were positive by norovirus-specific RT-PCR. Power and sample size not reported	

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Immunosuppressive therapy – 1.29; 0.79 Community acquired norovirus – 3.09; 0.06 *Multivariate analysis: All results OR (95% CI)* Age > 65 years – 11.56(1.89-224.00) Underlying malignancy – 0.02(0.00-0.19) Underlying trauma – 0.05(0.00-0.55) *POTASSIUM DECREASE >20%:* *Univariate analysis: All results OR; P value* Age > 65 years – 0.94; 1.00 Male gender – 0.90; 1.00 Underlying cardiovascular disorders – 5.17; 0.06 Underlying gastrointestinal disorders – 0.46; 0.67 Underlying autoimmune disease – 0.98; 1.00 Underlying renal disorders – 1.74; 0.71 Renal transplant – 3.91; 0.09 Underlying malignancy – P value 0.58; OR not reported Underlying trauma – P value 0.19; OR not reported Immunosuppressive therapy – 2.83; 0.25 Community acquired norovirus – 0.48; 0.68 *Multivariate analysis: All results OR (95% CI)* Underlying cardiovascular disorders – 17.10(2.17-403.00) Renal transplant – 13.02(1.63-281.00) *CREATININE INCREASE >10%:* *Univariate analysis: All results OR; P value* Age > 65 years – 1.04; 1.00 Male gender – 1.79; 0.24 Underlying cardiovascular disorders – 0.60; 0.42 Underlying gastrointestinal disorders – 1.93; 0.36 Underlying autoimmune disease – 4.50; 0.12 Underlying renal disorders – 1.44; 0.59 Renal transplant – 3.53; 0.07 Underlying malignancy – 0.93; 1.00 Underlying trauma – 0.07; <0.01 Immunosuppressive therapy – 5.74; <0.01 Community acquired norovirus – 5.07; 0.01 *Multivariate analysis: All results OR (95% CI)*		

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Immunosuppressive therapy – 5.67(1.78-20.1) *C REACTIVE PROTEIN >58 MG:* *Univariate analysis: All results OR; P value* Age > 65 years – 0.81; 0.79 Male gender – 2.63; 0.11 Underlying cardiovascular disorders – 0.32; 0.06 Underlying gastrointestinal disorders – 1.54; 0.55 Underlying autoimmune disease – 3.71; 0.14 Underlying renal disorders – 2.13; 0.19 Renal transplant – 1.33; 0.76 Underlying malignancy – 2.96; 0.25 Underlying trauma – 0.23; 0.35 Immunosuppressive therapy – 3.38; 0.06 Community acquired norovirus – 2.30; 0.23 *Multivariate analysis: All results OR (95% CI)* Underlying malignancy – 9.07(1.17-193.00) Immunosuppressive therapy – 5.37(1.62-19.9)		
Lopman, BA; 2004 [58]	Prospective controlled study 1,2,3,4	To describe norovirus outbreaks in residential homes or hospitals of principally older individuals.	Patients in hospitals and nursing homes in England. Cases were hospital patients, nursing home residents, and health care staff with ≥2 episodes of vomiting, ≥3 episodes of diarrhea, or both during a 24-hour period. Those with symptoms due to incontinence or ingestion of laxative drugs were excluded. 271 outbreaks – 33 in nursing homes and 238 in hospital units. 4378 cases – 2154 hospitalized patients, 1360 hospital care staff, 505 nursing home residents, and 358 nursing home	**Duration of symptomatic illness** Hospital patients vs. hospital staff, nursing home staff, and nursing home residents (75th percentile); p value – 3 days (5 days) vs. 2 days (3 days); p<0.001 Recovery was slowest in the oldest age group (≥85 years) of hospitalized patients - 40% symptomatic after 4 days	Outbreak is defined as ≥ 2 cases in a hospital functional care unit with dates of onset within 7 days of each other. Power and sample size not reported. Promotion of active surveillance (2-tiers of clinical symptoms) to detect cases as a means of prevention of outbreaks	642_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			staff.			
Rodriguez-Guillen, L; 2005 [60]	Prospective controlled study 2,4	To investigate the frequency of human CaCV (norovirus and sapovirus) in stool samples from adults and children with HIV.	Adults and children with and without HIV from Venezuela. Stool samples – 240 from adults and 81 from children. Subjects – 209 adults and 65 children.	**Detection in children vs adults; p value** CaCV – 62/159 vs 10/81; <0.0001 Novorivus GI – 4% detected exclusively from adults norovirus GII – 20% vs 4%; <0.01 **Detection in HIV positive vs negative subjects; p value** Adults – 22/108 vs 6/51; NS Children – 22/43 vs 9/38; 0.0111 **Detection in subjects with vs without diarrhea** HIV positive adults – 3/32 vs 10/76; 0.4234 HIV negative adults – 3/26 vs 3/25; 0.6468 HIV positive children – 11/18 vs 11/25; 0.2681 HIV negative children – 5/17 vs 4/21; 0.3565	Diarrhea defined as the occurrence of three or more bowel movements within a 24 hour period with decrease in stool consistency. Outcomes determined using RT-PCR. Power and sample size not reported.	502_IL
Lee, N; 2007 [59]	Retrospective controlled study 1,2,3,4,6,7	To study the association between fecal viral concentration and clinical manifestations of GII.4 norovirus infection. Risk factors for prolonged diarrhea were also studied.	Patients ≥16 yrs of age at 2 regional hospitals in Hong Kong. Mean age 60 years; 37.5% male. 44 enrolled; 40 analyzed	**Factors associated with higher median fecal viral concentration (during a 2 year study period)** *Univariate analysis (All results P value)* Age ≥ 65 yrs – 0.06 Female gender – 0.71 Pre-existing medical conditions – 0.52 Prolonged duration of diarrhea – <0.01 Frequency of vomiting – 0.22 Frequency of fever – 0.38 *Correlation analysis (All results Spearman correlation coefficient, P value)* Total duration of diarrhea – 0.47; <0.01 Total frequency of vomiting – 0.34; 0.04 **Risk factors for prolonged duration of diarrhea (during a 2 year study period)** *Univariate analysis (All results P value)* Age ≥ 65 yrs – <0.05 Pre-existing medical conditions – <0.05 Frequency of fever – 0.01 *Multivariate analysis (All results OR; 95% CI)* Fecal viral concentration (per log_{10} copies) – 9.56(1.18-77.57) Age (per year) – 1.15(1.03-1.28)	Cases were included for analysis if stool samples were collected ≤ 96 hours from symptom onset. Diarrhea was defined as having ≥ 3 loose stools per day. Diagnosis of norovirus infection and its quantitation were based on RT-PCR assay of stool samples. Prolonged diarrhea was defined as ≥ 4 days of diarrhea Power and sample size not reported Correlation between norovirus concentration and duration of illness (not severity)	2416_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
de Wit, M; 2003 [61]	Retrospective controlled study (nested case-control study) 1,3,4,6,7	To identify risk factors for norovirus infection	Patients registered at a general practice network in Netherlands. Cases were those persons identified in the community cohort with gastroenteritis and a matched control was selected from the cohort members without gastroenteritis at that time. Median age of case patients was 2 years. Other demographic characteristics were not reported. 152 case-control pairs	**Symptomatic norovirus infection** *All results OR(95% CI) unless otherwise noted* *All case-control pairs* *Univariate analysis* Poor food-handling hygiene (as a score) – 1.3(1.0-1.5); P<0.05 Low education level vs. intermediate education level – 1.9(0.9-4.0) High education level vs. intermediate education level – 2.2(1.2-3.9) Participant to day care center – 1.7(0.9-3.3) Household member to daycare center – 2.0(1.0-3.9) Household member to primary school – 1.6(1.0-2.7) Pets in household – 0.6(0.4-1.0) Cat as pet – 0.6(0.4-1.0) 1 household member with gastroenteritis vs. none – 3.7(1.7-8.0) >1 household member with gastroenteritis vs. none – 13.1(3.9-34.7) Child household contact – 5.2(1.8-15.3) Adult household contact – 4.4(2.0-9.6) Contact with person outside household with gastroenteritis – 11.4(4.7-27.3) Consumption of fish in the week before onset of symptoms – 1.8(1.0-3.2) Consumption of barbecued food in the week before onset of symptoms – 0.2(0.05-1.0) *Multivariate analysis* Poor food-handling hygiene (as a score) – 1.3(1.0-1.7); P<0.05 1 household member with gastroenteritis vs. none – 1.2(0.3-4.2) >1 household member with gastroenteritis vs. none – 10.9(2.0-60.5) Contact with person outside household with gastroenteritis – 12.7(3.1-51.8) *Population attributable risk (%) (based on multivariate odds ratios)* Poor food handling hygiene – 47 Number of household members with gastroenteritis – 17 Contact with person outside household with gastroenteritis – 56 *<1 year to 4 years (105 case-control pairs)* *Univariate analysis* Poor food-handling hygiene (as a score) – 1.2(0.9-1.5) ≥ 1 household members with gastroenteritis – 4.4(2.2-9.2) Contact with person outside household with gastroenteritis – 17.7(5.1-61.1) *Multivariate analysis* Poor food-handling hygiene (as a score) – 1.2(0.9-1.7)	Samples were tested for norovirus by RT-PCR Cases and controls were matched by age, degree of urbanization, region and date of inclusion Selection of variables into the multivariable model was backwards manually, based on the log likelihood ratio; a significance level of 0.05 was used. Food handling hygiene was determined using a questionnaire that included items on acquisition and preparation of food. Power and sample size not reported	763_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				≥ 1 household members with gastroenteritis – 2.7(0.8-8.9) Contact with person outside household with gastroenteritis – 10.9(2.2-54.6) *Population attributable risk (%) (based on multivariate odds ratios)* Poor food-handling hygiene (as a score) – 46 ≥ 1 household members with gastroenteritis – 27 Contact with person outside household with gastroenteritis – 51 *≥ 5 years (46 case-control pairs)* *Univariate analysis* Poor food-handling hygiene (as a score) – 1.3(0.9-1.9) ≥ 1 household members with gastroenteritis – 15.0(2.0-113.6) Contact with person outside household with gastroenteritis – 5.9(1.7-20.1) *Multivariate analysis* Poor food-handling hygiene (as a score) – 1.3(0.8-2.2) ≥ 1 household members with gastroenteritis – 1.1(0.1-15.9) Contact with person outside household with gastroenteritis – 12.1(1.0-147.3) *Population attributable risk (%) (based on multivariate odds ratios)* Poor food-handling hygiene (as a score) – 63 ≥ 1 household members with gastroenteritis – 4 Contact with person outside household with gastroenteritis – 60		
Gotz, H; 2001 [62]	Retrospective controlled study 1,3,4	To describe an outbreak in which secondary transmission into households by individuals occurred	Children and staff at 30 child centers (either a day care facility for preschool children or an after-school center for young children) in Sweden and their household contacts. Child center cases – 79 adults (mean age 41 yrs) and 114 children (mean age 5 yrs) Household cases – 58 adults (mean age 36 yrs) and 21 children (mean age 7 yrs) 775	**Symptoms** *All results adults vs. children - % reporting symptoms; P value* Diarrhea – 71.5 vs. 52.0; <0.01 Vomiting – 64.1 vs. 80.6; <0.01 Nausea – 96.8 vs. 93.1; 0.22 Stomach pain – 87.7 vs. 88.7; 0.82 Headache – 63.6 vs. 43.5; 0.01 Chills – 44.3 vs. 20.8; <0.01 Fever – 44.7 vs. 35.2; 0.20 Myalgia – 48.2 vs. 17.5; <0.01 **Symptomatic norovirus infection - Primary attack rate** Adults vs. children – 68/127 vs. 74/386; P<0.01 Children 0-5 yrs old vs. 6-10 yrs old – 44/204 vs. 30/179; P=0.23 **Symptomatic norovirus infection - Secondary attack rate** Adults vs. children – 11/59 vs. 40/312; P=0.23 Children 0-5 yrs old vs. 6-10 yrs old – 27/160 vs. 12/149; P=0.02	Primary case: a person in the child center who became ill and who had diarrhea, vomiting or nausea during the first 3 days of the outbreak Secondary case: a person who became ill from day 4 through day 12 of the outbreak Secondary household case: a person who became ill at >6 h but <10 days after the onset of disease in the corresponding patient who acquired the infection in the child center.	1024_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Risk factors for household transmission of symptomatic norovirus infection *All results RR(95% CI) unless otherwise noted* Children (vs. adults) – 3.8(1.9-7.6) Exposure to vomiting – 2.4(1.0-5.5) Exposure to diarrhea – 0.8(0.5-1.3) Increased frequency of vomiting – P<0.01 Size of household – P=0.14 Onset of illness at child center (vs. onset of illness at home) – 0.9(0.6-1.6) **Median incubation period for primary cases** 34 hours (range 2-61 hours) **Median serial interval** (between a case in the chid center and the linked household cases) Overall – 73 hours (range 4-198 hours) Counting only the first case in each household – 59 hours (range 4-198 hours) Truncating at 96 hours – 52 hours (4-96 hours)	Norwalk like virus (NLV) was confirmed using EM, used PCR for genotyping Power and sample size not reported 524/775 subjects (68%) returned the questionnaire	
Oppermann, H; 2001 [63]	Retrospective controlled study 1,2,3,4	To identify risk factors for a gastroenteritis outbreak.	Guests and staff at a mother and child health clinic in Germany. 166 guests and 49 staff met case definition. Data available for 164 guests and 47 staff.	**Symptomatic norovirus infection - Attack Rates** Guests 44% - adults 27% and children 54% Staff 23.4% **Symptomatic norovirus infection** *All results affected vs. not affected; p value* Children – 3.5 years vs. 6.3 years; <0.001 Adults – 32 years vs. 33 years; NS **Interventions** -At the start of each cure period guests should be instructed to wash hands after using the bathroom and prior to meals. Patients should immediately tell doctors about any gastrointestinal symptoms. -Persons with GI symptoms should have as little contact as possible with other guests of the health clinic and not use common facilities such as indoor swimming pools including cleaning personnel should be told immediately when GI disease is suspected and be given instructions about appropriate protective measures. -The rooms of the diseased persons, especially lavatories, should be cleaned daily using a virucidal disinfectant. Vomitus should be disinfected immediately.	Case definition was someone who stayed at the health clinic from October 27 to November 17, 1999 and had vomiting and/or diarrhea one day after his/her arrival at the earliest. NLV and astroviruses detected using PCR.	1041_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				-If an outbreak is suspected, the public health department should be notified.		
Sharp, TW; 1995 [64]	Retrospective controlled study 1,3,4,6,7	To identify risk factors for an outbreak onboard an aircraft carrier.	Crew members aboard an aircraft carrier. 4500 male crew members. Questionnaire results available for 2,618 shipboard personnel. Mean age 27 years (range, 17-59)	**Symptomatic norovirus infection - Attack rates (n=4500)** 13% with symptomatic infection 8% sought medical attention; almost all missed at ≥1 day work **Symptomatic norovirus infection** **Univariate analysis (n=2618)** *All results variable – attack rate; unadjusted OR (95% CI)* Age range (years) 17-19 – 17.6%; Reference 20-29 – 14.3%; 0.93 (0.6-1.5) 30-39 – 11.5%; 0.73 (0.4-1.2) 40-59 – 9.3%; 0.57 (0.3-1.2) Race White – 14.3%; Reference Black – 8.8%; 0.58 (0.4-0.85) Other – 17.2%; 1.24 (0.9-1.74) Rank Junior enlisted – 13.8%; Reference Senior enlisted – 10.7%; 0.74 (0.4-1.3) Officers – 9.4%; 0.65 (0.4-1.09) Number of persons in sleeping compartment 1-10 – 7.1%; Reference 11-50 – 8.6%; 1.23 (0.7-2.3) 51-100 – 15.5%; 2.39 (1.4-4.3) >100 – 18.6%; 2.98 (1.7-5.3) **Multivariate analysis (n=2618)** *All results variable – adjusted OR (95% CI)* Age (by year) – 0.98 (0.97-0.99) Race White – Reference Black – 0.6 (0.3-0.9) Other – 1.0 (0.7-1.3) Number of persons in sleeping compartment 1-10 – Reference 11-50 – 1.1 (0.5-1.7) 51-100 – 2.2 (1.6-2.8) >100 – 2.8 (2.3-3.4)	Power and sample size not reported. Gastroenteritis was defined as anyone reporting either vomiting or water stools with at least one of the following: nausea, fever, headaches, chills, or myalgias. Gastroenteritis was associated with at least a fourfold increase in Norwalk virus antibody levels measured by ELISA. Norwalk virus like particles were also seen using immune EM in 2/6 stools.	1513_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Pre-outbreak antibody levels and subsequent acute gastroenteritis *All results pre-outbreak antibody titer – No. developing illness/total No. (%)* <50 – 2/14 (14%) 50-200 – 9/28 (32%) 400-800 – 8/20 (40%) 1600-3200 – 11/35 (31%) ≥6400 – 2/12 (17%) All – 32/109 (29%) **Pre-outbreak antibody levels and subsequent fourfold or more titer rise** *All results pre-outbreak antibody titer – No. with fourfold or more titer rise/total No. (%)* <50 – 6/14 (43%) 50-200 – 12/28 (43%) 400-800 – 5/20 (25%) 1600-3200 – 9/35 (26%) ≥6400 – 2/12 (17%) All – 23/109 (31%) **Pre-outbreak antibody levels and subsequent fourfold or more titer rise with acute gastroenteritis** *All results pre-outbreak antibody titer – No. with fourfold or more titer rise and developing illness/total No. (%)* <50 – 2/14 (14%) 50-200 – 5/28 (18%) 400-800 – 4/20 (20%) 1600-3200 – 4/35 (11%) ≥6400 – 1/12 (8%) All – 16/109 (15%)		
Clinical characteristics						
Mattner, F; 2005 [56] 1,2,3	Systematic review	To investigate the effect of the index case (i.e., patient vs. staff) on infection risk and outbreak size.	All published nosocomial norovirus outbreaks with proven or suspected person-to-person transmission. Inclusion for statistical analyses limited to outbreaks with epidemic curves for each ward and outbreaks where the index case could be identified.	**Index case in outbreaks** Patient vs. staff – 20/30 (67%) vs. 10/30 (33%) **Symptomatic norovirus infection** *All results index case: patient vs.staff (95% CI for difference in mean); p value (30 wards included)* Mean number of affected patients – 27.75 vs 11.5 (5.1-27.0); 0.006 Mean number of affected staff – 11.75 vs 12.8 (-9.0 -6.9); 0.78 Mean number of overall affected individuals – 39.5 vs 24.3 (1.1-29.0); 0.36	Sources include Medline search from 1962-2004 using search terms: "norovirus", "Norwalk virus", "small round structured virus", and "outbreak"; Outbreak Worldwide Database; German data in Epidemiologisches Bulletin; data from personal	520_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			1033 individuals among 30 outbreaks included in the study.	*All results index case: patient vs. staff; OR (95% CI); p value (7 wards included)* Number of affected patients - 154/356 vs. 21/153; 4.79 (1.82-8.28); <0.0005 Number of affected staff – 79/224 vs. 36/136; 1.51 (0.92-2.49); 0.08	communication with a German teaching hospital; and author's own data. Power and sample size not reported.	
Mattner, F; 2006 [57]	Prospective controlled study 1,3,4,6,7	To characterize risk factors for the clinical complications of norovirus infections (e.g. vomiting, diarrhea, potassium decrease, creatinine increase, C-reactive protein increase)	All individuals working in or admitted to five wards (psychiatry, nephrology, gastroenterology, cardiology and trauma) at a university hospital in Germany in the period from the onset of clinical symptoms of the first patient until 2 days after the last patient became symptom free. All patients and staff members who were affected with a sudden onset of diarrhea and/or vomiting were included as cases. Patients admitted with clinical signs were regarded as index cases, and patients admitted ≥48 hrs before developing clinical signs were regarded as nosocomial cases 84 patients (72 acquired infection nosocomially) and 79 staff members (60 nurses). 3 norovirus positive patients were excluded from risk factor analysis. N for risk factor analyses was 53 for all outcomes except C	**Clinical features in patients** (study duration 3 months) Diarrhea – 79/84; 95% Vomiting – 57/84; 68% Somnolence – 2/84; 2% Serum creatinine increase > 10% – 22/84; 26% Serum potassium decrease > 20% – 7/84; 8% **Comparisons of attack rates in patients and nurses** (study duration 3 months) *All results are attack rate (%) in patients vs. nurses; P value* Psychaitry ward – 78 vs. 88; <0.01 Nephrology ward – 32% in the first period and 33% in the second period in patients. Data for nurses not given Gastroenterology – 27 vs. 90; <0.01 Cardiology – 42 vs. 44; 0.87 Trauma – 35 vs. 83; <0.01 Total – 38 vs. 76; <0.01 **Risk factors for complications of norovirus** (study duration 3 months) *VOMITING>1 DAY:* *Univariate analysis: All results OR; P value* Age > 65 years – 1.84; 0.30 Male gender – 0.91; 1.00 Underlying cardiovascular disorders – 2.7; 0.13 Underlying gastrointestinal disorders – 0.34; 0.31 Underlying autoimmune disease – 0.81; 1.00 Underlying renal disorders – 0.95; 1.00 Renal transplant – 1.31; 0.75 Underlying malignancy – P value 0.18; OR not reported Underlying trauma – 1.14; 1.00 Immunosuppressive therapy – 0.92; 1.00 Community acquired norovirus – 2.36; 0.19 *Multivariate analysis: All results OR (95% CI)*	Diarrhea was defined as three or more episodes of loose stools in a 24 hr period. Cases were considered to be norovirus-positive if samples from at least two patients from the same ward were positive by norovirus-specific RT-PCR. Power and sample size not reported	358_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			reactive protein increase (N=52)	Underlying cardiovascular disorders – 7.17(1.59-51.2) Community acquired norovirus – 5.54(1.04-42.8) *DIARRHEA>2 DAYS:* *Univariate analysis: All results OR; P value* Age > 65 years – 3.58; 0.01 Male gender – 2.15; 0.12 Underlying cardiovascular disorders – 2.80; 0.15 Underlying gastrointestinal disorders – 0.22; 0.03 Underlying autoimmune disease – 4.67; 0.24 Underlying renal disorders – 1.77; 0.39 Renal transplant – 1.71; 0.54 Underlying malignancy – 0.07; 0.01 Underlying trauma – 0.27; 0.053 Immunosuppressive therapy – 1.29; 0.79 Community acquired norovirus – 3.09; 0.06 *Multivariate analysis: All results OR (95% CI)* Age > 65 years – 11.56(1.89-224.00) Underlying malignancy – 0.02(0.00-0.19) Underlying trauma – 0.05(0.00-0.55) *POTASSIUM DECREASE >20%:* *Univariate analysis: All results OR; P value* Age > 65 years – 0.94; 1.00 Male gender – 0.90; 1.00 Underlying cardiovascular disorders – 5.17; 0.06 Underlying gastrointestinal disorders – 0.46; 0.67 Underlying autoimmune disease – 0.98; 1.00 Underlying renal disorders – 1.74; 0.71 Renal transplant – 3.91; 0.09 Underlying malignancy – P value 0.58; OR not reported Underlying trauma – P value 0.19; OR not reported Immunosuppressive therapy – 2.83; 0.25 Community acquired norovirus – 0.48; 0.68 *Multivariate analysis: All results OR (95% CI)* Underlying cardiovascular disorders – 17.10(2.17-403.00) Renal transplant – 13.02(1.63-281.00) *CREATININE INCREASE >10%:*		

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Univariate analysis: All results OR; P value Age > 65 years – 1.04; 1.00 Male gender – 1.79; 0.24 Underlying cardiovascular disorders – 0.60; 0.42 Underlying gastrointestinal disorders – 1.93; 0.36 Underlying autoimmune disease – 4.50; 0.12 Underlying renal disorders – 1.44; 0.59 Renal transplant – 3.53; 0.07 Underlying malignancy – 0.93; 1.00 Underlying trauma – 0.07; <0.01 Immunosuppressive therapy – 5.74; <0.01 Community acquired norovirus – 5.07; 0.01 *Multivariate analysis: All results OR (95% CI)* Immunosuppressive therapy – 5.67(1.78-20.1) *C REACTIVE PROTEIN >58 MG:* *Univariate analysis: All results OR; P value* Age > 65 years – 0.81; 0.79 Male gender – 2.63; 0.11 Underlying cardiovascular disorders – 0.32; 0.06 Underlying gastrointestinal disorders – 1.54; 0.55 Underlying autoimmune disease – 3.71; 0.14 Underlying renal disorders – 2.13; 0.19 Renal transplant – 1.33; 0.76 Underlying malignancy – 2.96; 0.25 Underlying trauma – 0.23; 0.35 Immunosuppressive therapy – 3.38; 0.06 Community acquired norovirus – 2.30; 0.23 *Multivariate analysis: All results OR (95% CI)* Underlying malignancy – 9.07(1.17-193.00) Immunosuppressive therapy – 5.37(1.62-19.9)		
Lopman, BA; 2004 [58]	Prospective controlled study 1,2,3,4	To describe norovirus outbreaks in residential homes or hospitals of principally older individuals.	Patients in hospitals and nursing homes in England. Cases were hospital patients, nursing home residents, and health care staff with ≥2 episodes of vomiting, ≥3 episodes of	**Duration of illness** Hospital patients vs. hospital staff, nursing home staff, and nursing home residents (75th percentile); p value – 3 days (5 days) vs. 2 days (3 days); p<0.001 Recovery was slowest in the oldest age group (≥85 years) of hospitalized patients - 40% symptomatic after 4 days	Outbreak is defined as ≥ 2 cases in a hospital functional care unit with dates of onset within 7 days of each other. Power and sample size not reported.	642_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			diarrhea, or both during a 24-hour period. Those with symptoms due to incontinence or ingestion of laxative drugs were excluded. 271 outbreaks – 33 in nursing homes and 238 in hospital units. 4378 cases – 2154 hospitalized patients, 1360 hospital care staff, 505 nursing home residents, and 358 nursing home staff.		Promotion of active surveillance (2-tiers of clinical symptoms) to detect cases as a means of prevention of outbreaks	
Rodriguez-Guillen, L; 2004 [60] Prospective controlled study 2,4	To investigate the frequency of human CaCV (norovirus and sapovirus) in stool samples from adults and children with HIV.	Adults and children with and without HIV from Venezuela. Stool samples – 240 from adults and 81 from children. Subjects – 209 adults and 65 children.	**Detection in children vs adults; p value** CaCV – 62/159 vs 10/81; <0.0001 Novorivus GI – 4% detected exclusively from adults norovirus GII – 20% vs 4%; <0.01 **Detection in HIV positive vs negative subjects; p value** Adults – 22/108 vs 6/51; NS Children – 22/43 vs 9/38; 0.0111 **Detection in subjects with vs without diarrhea** HIV positive adults – 3/32 vs 10/76; 0.4234 HIV negative adults – 3/26 vs 3/25; 0.6468 HIV positive children – 11/18 vs 11/25; 0.2681 HIV negative children – 5/17 vs 4/21; 0.3565	Diarrhea defined as the occurrence of three or more bowel movements within a 24 hour period with decrease in stool consistency. Outcomes determined using RT-PCR. Power and sample size not reported.	502_IL
Thea, D; 1993 [65] Prospective controlled study 1,3,4	To determine the prevalence of enteric viruses and their relation to diarrhea, wasting and immunosuppression among HIV infected and uninfected persons.	Adult general medical patients admitted to a hospital in Zaire. 57% were HIV positive. 10/198 patients had SRSV infection. 234 enrolled, 198 analyzed	**Presence of diarrhea in patients shedding norovirus** Of 10 patients shedding norovirus, 2 had acute diarrhea, 2 had chronic diarrhea and 6 had no diarrhea **Presence of HIV infection in patients shedding norovirus** Of 10 patients shedding norovirus, 5 had HIV infection (1 Stage III and 4 Stage IV) and 5 did not. **Asymptomatic norovirus infection - Viral shedding** *Association with HIV infection* HIV positive vs. HIV negative – 17% vs. 18%; P=0.82	norovirus was detected by EM. HIV Stages: I: Asymptomatic II: Mild disease III: Moderate disease IV: Acquired immune deficiency syndrome (AIDS) Power and sample size not	1606_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Viral shedding vs. no viral shedding (Stage III HIV positive) – P=0.80 Viral shedding vs. no viral shedding (Stage IV HIV positive/AIDS) – P=0.79 *Association with degree of immunocompromise (defined by CD4/CD8 ratio)* *All results P values for test of trend towards greater frequency of shedding among lower CD4/CD8 quintiles* Overall – P=0.14 Among HIV positive – 0.07 Among HIV negative – 0.45	reported	
Lee, N; 2007 [59]	Retrospective controlled study 1,2,3,4,6,7	To study the association between fecal viral concentration and clinical manifestations of GII.4 norovirus infection. Risk factors for prolonged diarrhea were also studied.	Patients ≥16 yrs of age at 2 regional hospitals in Hong Kong. Mean age 60 years; 37.5% male. 44 enrolled; 40 analyzed	**Factors associated with higher median fecal viral concentration (during a 2 year study period)** *Univariate analysis (All results P value)* Age ≥ 65 yrs – 0.06 Female gender – 0.71 Pre-existing medical conditions – 0.52 Prolonged duration of diarrhea – <0.01 Frequency of vomiting – 0.22 Frequency of fever – 0.38 *Correlation analysis (All results Spearman correlation coefficient, P value)* Total duration of diarrhea – 0.47; <0.01 Total frequency of vomiting – 0.34; 0.04 **Risk factors for prolonged duration of diarrhea (during a 2 year study period)** *Univariate analysis (All results P value)* Age ≥ 65 yrs – <0.05 Pre-existing medical conditions – <0.05 Frequency of fever – 0.01 *Multivariate analysis (All results OR; 95% CI)* Fecal viral concentration (per log_{10} copies) – 9.56(1.18-77.57) Age (per year) – 1.15(1.03-1.28)	Cases were included for analysis if stool samples were collected ≤ 96 hours from symptom onset. Diarrhea was defined as having ≥ 3 loose stools per day. Diagnosis of norovirus infection and its quantitation were based on RT-PCR assay of stool samples. Prolonged diarrhea was defined as ≥ 4 days of diarrhea Power and sample size not reported Correlation between norovirus concentration and duration of illness (not severity)	2416_RA
Marx, A; 1999 [66]	Retrospective controlled study 1,3,4	To assess risk factors for gastroenteritis associated with Norwalk-like viruses (NLVs)	Residents and employees at a geriatric long term care facility. 68% residents were female, median age was 83 yrs (range 65-106). 78% of employees were female, median age was 36 yrs. Study was	*All results RR(95% CI); P value for the presence of risk factor* **Risk factors for symptomatic norovirus infection among residents** Physical dependence – 3.5(1.0-12.9);0.02 Respiratory therapy – 2.3(0.8-6.4); 0.20 Antibiotics – 1.6(1.0-2.8); 0.20 Chronic infections – 1.6(0.9-3.0); 0.40 Tube feeding – 1.3(0.7-2.6); 0.70 Disoriented – 1.2(0.8-1.8); 0.60	A case of acute gastroenteritis was defined as an individual with onset of vomiting or diarrhea during the study period (Feb 12 – Mar 20 1996); diarrhea was defined as ≥2 loose or watery stools in a 24 hr	1237_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			conducted in Washington State. 91 residents and 97 employees	Diuretics – 0.4(0.2-0.9); 0.02 **Risk factors for symptomatic norovirus infection among employees** Exposure to vomitus – 2.6(1.1-6.5); 0.03 Gastroenteritis in household – 2.3(1.4-3.6); 0.01 Exposure to residents with gastroenteritis – 2.2(1.0-4.9); 0.05 Resident care – 1.4(0.8-2.5); 0.30 Tap water – 0.9(0.5-1.5); 0.60 Ice – 0.7(0.4-1.2); 0.20 **Symptomatic norovirus infection (Effect of protective measures among nursing staff)** Gowning – 0.4(0.1-1.4) Strict hand washing – 0.7(0.2-1.3) Use of hand-disinfection gel – 0.8(0.4-1.4) Laundering work clothes daily – 1.2(0.7-1.3)	period. A single NLV strain of genogroup II genetically related to Toronto virus was the only pathogen identified. NLVs were identified by EM in stool and vomitus specimens and further characterized by RT-PCR and nucleotide sequencing. Data on residents was collected through medical records. 90 of 97 employees completed a self-administered questionnaire Power and sample size not reported	
Caceres, V; 1998 [67]	Retrospective controlled study 1,3,4	To identify the etiologic agent and risk factors associated with a hospital ward outbreak of gastroenteritis.	Patients and staff on a medical-surgical ward in South Carolina where the index case (a nursing staff member) worked. Overall demographics not reported. 89 staff and 91 patients	**Symptomatic norovirus infection - Attack rate** (during the study period) Staff vs. patients – 28/89 vs. 10/91; RR(95% CI) = 2.9(1.5-5.5) **Symptomatic norovirus infection among staff** *All results RR(95% CI) (comparisons not clear, assume the opposite of the risk factor given)* Stayed in hospital overnight – 2.0(1.0-3.9) Assisted ill patients – 1.1(0.6-2.2) Worked longer hours – 1.8(1.0-3.5) Used staff bathroom on ward – 22/61 vs. 0/1; RR undefined Ate in cafetaria – 1.5(0.7-3.1) Brought own food – 1.1(0.6-2.1) Consumed water from ward – 1.4(0.7-2.8) Consumed ice from ward – 1.1(0.2-5.5) Changing bed sheets without golves – 1.7(0.7-4.0) Changing urine catheters without gloves – 0/0 vs. 17/54; RR undefined Turning patients without gloves – 0.8(0.4-1.9) **Symptomatic norovirus infection among household members** Case staff vs. non-case staff – 5/27 vs. 7/69; 1.8(0.6-5.3) **Symptomatic norovirus infection among patients** *All results RR(95% CI) (comparisons not clear, assume the opposite of the*	A case was defined as a staff member or patient who had acute onset of vomiting and diarrhea from January 5-13, 1996 as recorded in patient charts. A patient was considered to be exposed if he or she had been taken care of by a case-nurse (an assigned nurse who was a primary caretaker) who had developed the illness in the preceding 48 hours. Staff exposure was ascertained if care of a symptomatic patient occurred within 48 hours All stool and vomit specimens were obtained within 48 hours after the	1324_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				risk factor given) ED vs. admitted directly from home – 1.3(0.4-4.5) Regular diet - 1.4(0.4-4.4) Full ambulation – 2.6(0.7-9.5) Physical therapy – 0.8(0.2-2.9) Urinary catheter care – 1.2(0.4-4.0) Nasogastric tube care – 0/5 vs. 10/86; RR undefined Wound care – 0/24 vs. 10/67; RR undefined Respiratory care – 5.7(1.8-18.1) **Risk of symptomatic norovirus infection associated with patient nurse exposures** *All results RR(95% CI)* Patients – on a shift with an assigned primary nurse who had onset of illness in the preceding 48h vs. not – 14% vs. 0%; RR undefined Nurses – on a shift with an assigned primary patient who had onset of illness in the preceding 48h vs. not – 0.3(0.1-1.1) **Discharge diagnoses of vomiting, diarrhea or viral gastroenteritis** Month of outbreak vs. same month previous year – 79/3567 vs. 63/3982; P<0.05 **Etiologic agent** EM identified SRSV in 9 of 9 stool samples	onset of gastroenteritis. Specimens were examined by EM for viral particles and by RT-PCR for SRSV RNA Power and sample size not reported	
Cegielski, J; 1994 [68]	Controlled study based on a cross-sectional survey None	To determine whether specific viruses were associated with HIV infection	HIV infected and HIV uninfected Tanzanian children admitted with chronic diarrhea, and controls without diarrhea aged 15 months to 5 years. Consecutive sample (n=59) Not reported	**Asymptomatic norovirus infection** HIV infected children with chronic diarrhea vs. HIV uninfected children with chronic diarrhea – 4/21 vs. 1/32; Prevalence Ratio (90% CI) – 6.09(1.03-36.14) Rotavirus and coronavirus particles were not associated with HIV infection.	Enteric viruses were identified by EM of fecal specimens. Asymptomatic infection defined as presence of SRSV Power and sample size not reported	1525_RA
Laboratory Characteristics						
Halperin, T; 2008[69]	Prospective controlled study 1,3,4	To determine if norovirus genogroup II susceptibility is related to ABO phenotype.	Sick soldiers and healthy contacts in military units in Israel during outbreaks during February 2003 and January 2005. All soldiers	**Symptoms** Attack rate – 20%. Nausea and/or emesis – 75% Diarrhea – 69% Stomachache – 65% Fever – 17%	Cases had emesis, nausea, or stomachache. Healthy contacts served in the same company as the	5114_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			were male and 18-22 years old. 138 cases and 166 healthy subjects.	**ABO distribution** A – 36.5% AB – 11.8% B – 20% O – 31.6% **Risk Factor compared to blood type O** *All results – Symptomatic infection OR (95% CI); Fever OR (95% CI)* A – 0.58 (0.33-1.01); 2.14 (0.68-6.74) AB – 0.48 (0.20-1.14); OR N/A B – 0.72 (0.37-1.38); 3.08 (0.89-10.67)	case patients, had no GI symptoms, and were in the compound for at least the 3 days prior to the outbreak. Power and sample size not reported.	
Hutson, A; 2005 [70]	Prospective controlled study 1,2,3,4	To evaluate whether secretor status was associated with resistance to norovirus infection.	Volunteers experimentally challenged with norovirus. Demographic characteristics not reported. Study was conducted in Texas. 51	**Asymptomatic norovirus infection (following challenge)** Secretor positive vs. secretor negative – 42/43 vs. 0/8; statistical differences were not reported **Symptomatic norovirus infection (following challenge)** Secretor positive vs. secretor negative – 29/43 vs. 0/8; statistical differences were not reported	norovirus infection was defined as four-fold or greater increase in norovirus specific serum antibody titer (ELISA) or norovirus antigen shedding [ELISA, radioimmunoasay (RIA) or RT-PCR] Secretor genotype was assessed by testing PCR products obtained from deoxyribonucleic acid (DNA) extracted from archived sera. FUT2 gene typically associated with non-secretor status (norovirus resistant) and in 20% of Caucasians. Study did not characterize participants by ethnicity, only FUT2 genotyping. Power and sample size not reported	468_RA
Thorven, M; 2005 [71]	Prospective Controlled Study	To investigate if the FUT2 secretor gene was associated with	Symptomatic and asymptomatic individuals from nosocomial and	**Secretor Status** Outbreak 1 (Internal Medicine Ward; N=50) *Symptomatic patients:*	A patient with gastroenteritis was defined as a patient with vomiting (≥ once/24 h)	400_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
	1,3,4	resistance to nosocomial and sporadic outbreaks caused by genogroup II noroviruses	sporadic outbreaks of genogroup II norovirus. Blood donors in Sweden were used as a second control group. Patient demographics not described. Study was conducted in Sweden. 115	Homozygous secretors – 47% Heterozygous secretors – 53% Secretor negative – 0% *Asymptomatic patients:* Secretor negative – 19% (Number of patients for each category was not reported) Outbreak 2 (Pediatrics Ward; N=28) *Symptomatic patients:* Secretor negative – 0/7 *Asymptomatic patients:* Secretor negative – 9/21 Outbreak 3 (Orthopedic Ward; N=18) *Symptomatic patients:* Secretor negative – 0/12 *Asymptomatic patients:* Secretor negative – 3/6 Community Outbreaks (N=19) *Symptomatic patients:* Homozygous secretors – 7/15 Heterozygous secretors – 8/15 Secretor negative – 0/15 *Asymptomatic patients:* Homozygous secretors – 2/4 Heterozygous secretors – 2/4 Secretor negative – 0/4 Cumulative data Homozygous non secretor status Symptomatic patients vs. non-symptomatic patients – 0/53 vs. 18/62; P<0.01 Symptomatic patients vs. blood donors – 0/53 vs. 21/104; P<0.01	and/or diarrhea (≥ 2 watery stools/24 h) norovirus was detected in stool using RT-PCR. The DNA from saliva was sequenced for secretor genotype using sequence-specific primers and PCR. Power and sample size not reported	
Lindesmith, L; 2003 [72]	Prospective controlled study 1,2,3,4	To investigate the role of secretor status and acquired immunity in Norwalk virus infection. Volunteers received doses of Norwalk virus inoculum ranging from 10 to 3 × 10^8 PCR	Volunteers dosed with Norwalk virus. 49% male; 71% white, 23% black and 6% other races; average age 30 yrs (range 20-49). Study was conducted in North Carolina.	**Asymptomatic norovirus infection (following challenge)** Secretor positive vs. secretor negative – 34/55 vs. 0/22; P<0.01 Blood types Among O blood type Secretor positive – RR 1.56; P<0.05 Secretor negative – No events; P>0.05 Overall – RR 1.89; P<0.05	Norovirus infection was defined as viral RNA detected in stool or a ≥4-fold increase in Norwalk-virus specific serum IgG. Symptomatic infection was defined as an infected subject with vomiting or	830_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
		detectable units.	77	Among A blood type Secretor positive – RR 0.79; P>0.05 Secretor negative – No events; P>0.05 Overall – RR 0.54; P<0.05 Among B blood type Secretor positive – RR 0.66; P>0.05 Secretor negative – No events; P>0.05 Overall – RR 0.82; P>0.05 Among AB blood type Secretor positive – No events; P>0.05 Secretor negative – No events; P>0.05 Overall – P>0.05 **Symptomatic norovirus infection** O blood type– P>0.05	diarrhea (>2 unformed stools in 24 hours). Secretor genotype was determined through PCR amplification of DNA extracted from saliva. Data on immunity was not not extracted as it was not clinically relevant (antibody titers) Comparison group for RR unclear. Power and sample size not reported	
Hutson, A; 2002 [73]	Prospective controlled study 1,2,3,4	To investigate the role of ABO phenotype in norovirus susceptibility	Volunteers experimentally challenged with norovirus. Demographic characteristics not reported. Study was conducted in Texas. 51	*All results OR (95% CI); P value by Fisher's exact for the presence of blood type and the risk of infection* **Asymptomatic norovirus infection (following challenge)** O – 11.80(1.3-103.00); 0.01 A – 0.63(0.14-2.70); 0.70 B – 0.27(0.04-1.90); 0.21 AB – 0(0-1.10); 0.03 A/AB combined – 0.25(0.05-1.20); 0.13 B/AB combined – 0.10(0.02-0.56); 0.01 **Symptomatic norovirus infection (following challenge)** O – 0.89(0.23-3.40); 1.0 A – 3.90(0.72-21.00); 0.16 B – 0(0-0.99); 0.03	norovirus infection was defined as four-fold or greater increase in norovirus specific serum antibody titer (ELISA) or norovirus antigen shedding (ELISA, RIA or RT-PCR) Asymptomatic infection was defined as the absence of vomiting and/or diarrhea and a low overall symptom score (abdominal cramps, chills, body ache, headache, nausea and fever) Comparison group for OR unclear. Power and sample size not reported	954_RA
Graham DY, 1994[74]	Prospective controlled	To evaluate the clinical features and virologic	8 volunteer studies between July 1985 and	**Infection status measured by serum antibody response** After norovirus challenge, 9 (18%) uninfected vs. 41 (82%) infected.	ELISA to detect norovirus specific antibodies and	1563_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
	study 1,3,4	and immunologic responses following oral administration of Norwalk virus.	January 1990 where medical students and staff of the Texas Medical Center were administered norovirus. 21 women, 30 men 19-39 years old 43 white, 6 black, 1 Hispanic, and 1 East Indian. N=50 subjects	Of those infected, 82% with vs. 60% without preexisting antibody; p>0.2. Of those infected, Group 4 subjects had higher preexisting antibody titers than uninfected subjects; p=0.004 Uninfected subjects had lower preexisting antibody titers than infected subjects; p<0.001 Of those infected, there were increases in geometric mean titers after infection (p<0.01) and the increase in convalescent titers were higher in subjects with vomiting (Groups 3 and 5 vs. 2 and 4; p=0.016) or with vomiting and diarrhea (Group 5 vs. 2-4, p=0.02) *All results: No (%) subjects with pre-existing Norwalk virus antibody titers of levels <10 vs. 10 vs. 40 vs. 160 vs. 640 vs 2560 who have the characteristic of interest* Seroconversion: 3/5 (60) vs. 4/7 (57) vs. 13/17 (76) vs. 16/16 (100) vs. 4 /4(100) vs. 0/1; p value=0.065 Viral shedding: 2 (40) vs. 2 (29) vs. 12 (70) vs. 16 (100) vs. 3 (75) vs 1 (100); p value=0.0012 Diarrhea: 2 (40) vs. 1 (14) vs. 10 (59) vs. 7 (44) vs. 3 (75) vs. 1 (100); p value=NS Vomiting: 2 (40) vs. 1 (14) vs. 7 (41) vs. 5 (31) vs. 1 (25) vs 0; p value=NS Nausea: 2 (40) vs. 1 (14) vs. 11 (65) vs. 10 (62) vs. 4 (100) vs. 0; p=0.065 Cramps: 2 (40) vs. 1 (14) vs. 12 (70) vs. 10 (62) vs. 2 (50) vs. 0; p value=NS Headache: 4 (80) vs. 3 (42) vs. 12 (70) vs. 9 (56) vs. 3 (75) vs. 0; p value=NS Chills: 1 (20) vs. 0 vs. 5 (29) vs. 3 (19) vs. 1 (25) vs. 0; p value=NS Fever: 1 (20) vs. 0 vs. 4 (23) vs. 3 (19) vs. 1 (25) vs. 0; p value=NS ***Virologic parameters of infection*** 64% patients with symptomatic infection vs. 32% with asymptomatic infection had stools with positive antigen Earliest positive sample occurred at 15 hours Peak of stool viral shedding 25-72 hours after inoculation Most infected volunteers shed viral antigen continuously from their first positive sample until the last sample obtained Longest antigen shedding was 7 days after inoculation and 1 asymptomatic subject shed antigen 6 days after inoculation *All results No. positive/no. tested stool samples (%); Mean no. stools/person/day in Uninfected vs. Infected (asymptomatic) vs. Infected (symptomatic) patients at different time points* Day 0: 0/5; 0.6 vs. 0/7; 0.5 vs. 0/10; 0.4 Day 1: 0/6; 0.7 vs. 0/16; 1.2 vs. 12/51 (24); 1.8	antigen in stool. Biotin-avidin ELISA, RIA, RT-PCR, and dot blot hybridization to detect antigen in stool. Norovirus infection defined as ≥ 4 fold increase in serum antibody titer or excretion of virus. Diarrhea defined as watery stools (unformed stools not considered diarrhea). Asymptomatic infection defined as no vomiting or diarrhea and a symptom score of ≤4 in an infected subject. Symptomatic infection defined as a composite symptom score of ≥ 5 in an infected subject. Patients who vomited or had diarrhea had symptomatic infection. Subjects divided into 5 groups: Group 1 - uninfected Group 2 - asymptomatic or mildly symptomatic (no vomiting or diarrhea) Group 3 - symptomatic (vomiting but no diarrhea) Group 4 - symptomatic (no vomiting but watery diarrhea) Group 5 - symptomatic (vomiting and watery diarrhea)	

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Day 2: 0/7; 0.8 vs. 9/17 (53); 1.3 vs. 81/109 (74); 3.9 Day 3: 0/13; 1.4 vs. 5/9 (56); 0.7 vs. 40/44 (91); 1.6 Day 4: 0/1; NC vs. 2/3 (67); NC vs. 16/22 (73); NC Day 5: 0/4; NC vs. 1/3 (33); NC vs. ½ (50); NC Day 6: 0/2; NC vs. 1/1 (100); NC vs. 5/5 (100); NC Day 7: 0/1; NC vs. NS; NC vs. 2/2 (100); NC Total: 0/39; NC vs. 18/56 (32); NC vs. 157/245 (64); NC NC - not calculated because not all stools collected after subjects discharged NS – no samples received. ***Clinical features of subjects relative to infection status*** Incubation time to onset of symptoms: 24-38 hours Duration of illness: 2-3 days Diarrhea: occurred earliest at 15 hours and latest at 55 hours after inoculation. *All results: No. (%) subjects with antibody responses 0 vs. 4 vs. 16 vs. 64 vs. 256 fold with the characteristic of interest; total No. subjects with antibody response* Diarrhea: 1/10 (10) vs. 0/3 vs. 9/15 (60) vs. 11/17 (65) vs. 3/5 (60); 24/50 (59); p value=NS Vomiting: 0 vs. 0 vs. 4 (27) vs. 9 (53) vs. 3 (60); 16 (39); p value=0.02 Nausea: 1 (10) vs. 0 vs. 10 (67) vs. 13 (76) vs. 4 (80); 27 (66); p value≤0.02 Cramps: 0 vs. 1 (33) vs. 10 (67) vs. 12 (71) vs. 4 (80); 27 (66) ; p value=NS Headaches/body aches: 4 (40) vs. 0 vs. 11 (73) vs. 12 (71) vs. 4 (80); 27 (66); p value=0.04 Chills: 0 vs. 0 vs. 4 (27) vs. 5 (29) vs. 1 (20); 10 (24); p value=0.08 Fever: 0 vs. 0 vs. 3 (20) vs. 3 (18) vs. 3 (60); 9 (22) ; p value=NS **Antigen vs. antibody detection** *All results: Patients with given clinical scores who had the following antigen response/antibody response (+/+ vs -/+ vs +/- vs. -/-)* Clinical score 0-2 (uninfected): 0 vs 0 vs 0 vs 9 Clinical score 0 (asymptomatic infection): 4 vs 4 vs 0 vs 0 Clinical score 1-4 (mild symptomatic infection): 4 vs 1 vs 0 vs 0 Clinical score 5-24: 26 vs 1 vs 1 vs 0 Total: 34 vs 6 vs 1 vs 9 Antibody detection may be more sensitive than antigen detection	Clinical scores: symptoms were graded using a 5 point score with 0 (absence of symptom) and 5 (most severe iscomfort with symptom). Compositescores tabulated for 72 hour period after inoculation (maximum score 35). Power and sample size not reported.	
Nakata, S; 1985 [75]	Prospective controlled	To determine if clinical illness correlates with	Human CaCV outbreak in a Japanese orphanage	**Symptomatic infection** Preexisting serum CaCV antibody – present 3/18 vs. absent 18/23; p<0.01	All patients except one, who only had vomiting, had	1960_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
	study 1,2,3	pre-existing CaCV serum antibody.	during October 1982. 41		diarrhea. Power and sample size not reported.	
Parrino, TA; 1977 [76]	Prospective controlled study 1,2,3,4,5	To examine immunity in viral gastroenteritis.	Male volunteers, 30-47 years of age, were challenged with Norwalk virus and had symptoms, jejunal biopsies, and serum antibodies evaluated. 12	**Baseline** All subjects had normal baseline biopsy samples. **First challenge** 6/12 developed gastroenteritis. 4/5 symptomatic volunteers who had antibody levels checked had increase in serum Norwalk antibodies that waned over time. 3/3 asymptomatic patients who had antibodies checked did not have increase in serum antibody. 3/5 symptomatic volunteers had abnormal biopsies. 2/5 asymptomatic volunteers had normal biopsies. **Second challenge** (27-42 months later) 6/12 who were symptomatic after the first challenge were symptomatic again with jejunal lesions after the second challenge. 6/12 who were previously asymptomatic were asymptomatic without jejunal lesions. 3/3 asymptomatic patients who had antibody levels checked did not have increase in serum antibody. **Third challenge** *Only performed in 4/6 volunteers who twice became symptomatic; 4-8 weeks after second challenge* 1 was symptomatic. 3 were asymptomatic.	Patients were considered clinically ill if they had vomiting and/or diarrhea with one or more associated signs and symptoms. Two investigators characterized subjects as clinically ill without knowledge of serologies or small bowel biopsy results. Two investigators characterized subjects without knowledge of serologic findings and prior to biopsy results. Immune-electron-microscopy technique was performed for measurement of Norwalk serum antibody using the 8FIIa Norwalk filtrate as antigen. Power and sample size not reported.	2228_IL
Fretz, R; 2005 [77]	Retrospective controlled study 1,2,3,6,7	To identify risk factors for sporadic norovirus infections.	All patients of general practitioners in German-speaking parts of Switzerland. Cases (mean age 32.7 years; median age 34 years; range 1.1-69.3 years) were subjects who resided in the study area who had an episode of diarrhea and/or vomiting,	**Symptoms** (study duration 2 years) Diarrhea – 124/126 (98.4%). Vomiting – 84/126 (66.7%). Nausea – 85/126 (67.5%) Fever – 57/126 (45.2%) Headache – 45/126 (35.7%) Abdominal cramps – 87 (69%) Other – 46 (36.5%) **Mean duration of symptomatic illness** 7.3 days (SD, 6.2 days; range 0.25-28 days)	Power and sample size reported as 70 matched case-control pairs to detect an OR of 2.9 (alpha 0.05; power 0.80; 0.5 probability of an event in the exposed group). Period between the start of symptoms and completion of the patient questionnaire	506_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			consulted a practitioner in the study area, had stool samples negative for *Campylobacter, Shigella, Salmonella*, and other gastroenteric pathogens, had stool samples positive for norovirus genogroup I or II. Cases excluded subjects <6 months or >75 years, patients with possible nosocomial disease, and patients who were part of a norovirus outbreak. Controls (mean age 33.2 years; median age 37.1 years; range 1.3-70.1 years) were identified through each patient, were the same sex and age group (defined as 5 year intervals over 5-20 years and 10 year intervals over 20-60 years), lived within 10 kilometer (km) of the case, and had not consulted a general practitioner for gastrointestinal illness or symptoms in the month prior to the questionnaire. 126 cases met study inclusion criteria. 73 matched case-control pairs.	**Symptomatic norovirus infection** *Multivariable analysis* *Consumption of food and beverages OR (95% CI); p value* Mineral water – 1.00 (0.46-2.16); 1.00 Salad – 1.25 (0.34-2.65); 0.74 Raw berries – 0.75 (0.17-3.35); 0.71 Tap water – 1.33 (0.56-3.16); 0.51 Sweet beverages – 1.06 (0.55-2.05); 0.87 *Personal contacts OR (95% CI); p value* Household with children ≤2 years) – 1.00 (0.29-3.45); 1.00 Household with children ≤ 5 years – 0.75 (0.26-2.16); 0.59 Household with children ≤ 10 years – 0.75 (0.26-2.16): 0.59 Household with children ≤ 65 years – 0.75 (0.17-3.35); 0.71 Household with children > 1 person – 1.50 (0.53-4.21); 0.44 Household with children > 2 person – 0.77 (0.34-1.75); 0.53 Household with children > 3 person – 0.71 (0.32-1.61); 0.53 Household with children > 4 person – 1.14 (0.41-3.15); 0.53 **Symptomatic norovirus infection** *ABO histo-blood group OR (95% CI); p value - conditional logistic regression* Type A: 1.34 (0.55-3.42); 0.49 Type B: 0.33 (0.07-1.65); 0.15 Type O: 1.00 (0.40-2.52); 0.49 Type AB: 1.50 (0.25-8.98); 0.65 Type A/AB: 1.44 (0.62-3.38); 0.39 Type B/AB: 0.63 (0.20-1.91); 0.40 **Symptomatic norovirus infection** *ABO histo-blood group OR (95% CI)*; p value – *random effects logistic regression* Type A: 1.20 (0.55-2.61); 0.64 Type B: 0.28 (0.07-1.13); 0.07 Type O: 1.11 (0.51-2.45); 0.79 Type AB: 1.89 (0.35-10.2); 0.46 Type A/AB: 1.39 (0.64-3.00); 0.40 Type B/AB: 0.59 (0.21-1.70); 0.32	averaged 29 days (median 24 days).	
Meyer, E; 2004 [78]	Retrospective controlled study	To determine if O phenotype is more commonly found in	Cases were subjects with vomiting, nausea, and/or diarrhea from two	**Symptomatic norovirus infection** *% blood donors vs. % outbreaks with particular ABO phenotype; p value* Type O – 41.2 vs. 22; 0.01	Power and sample size not reported.	729_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
	1,2,3,4	patients from norovirus outbreaks compared to blood donors.	nosocomial norovirus outbreaks at a German university hospital. Controls were blood donors in Southwest Germany. 95 cases and 45 controls.	Type A – 43.3 vs 58; 0.52 Type B – 10.7 vs 11; 1.00 Type AB – 4.8 vs 9; 0.34		

Virus characteristics

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
Tu ET, 2008 [108]	Descriptive study 3,4	To describe the emergence of new GII.4 variants during the early 2006 epidemic period in Australia and New Zealand.	Fecal samples from gastroenteritis outbreaks in Australia and New Zealand in early 2006. 231 fecal samples were obtained from patients with acute gastroenteritis from Australia and New Zealand through the surveillance network between December 2005 through August 2006. 87 outbreaks. N=186 sequenced samples.	***norovirus genotype (%) in outbreaks*** GII.2 (0.5%) GII.3 (9%) GII.4 (86%) GII.5 (0.5%) GII.12 (2%) GII.16 (2%) ***Genotype (%) by Location*** ***New South Wales, Australia (n=119 sequenced strains)*** GII.4 2006a (57.1%) GII.4 2006b (17.6%) GII.4 US95/96 (13.4%) GII.4 Hunter (2.5%) GII.b/GII.3 (4.2%) GII.3 (1.7%) GII.4/GII.12 (2.5%) GII.2 (08%) ***Queensland, Australia (n=11)*** GII.b/GII.3 (45.5%) GII.3 (36.3%) GII.4 2006a (18.2%) ***Victoria, Australia (n=14)*** GII.4 2006a (100%) ***New Zealand (n=42)***	Fecal samples tested using RT-PCR. Power and sample size not reported.	5120_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				GII.4 2006a (73.8%) GII.4 Hunter (11.9%) GII.16 (7.1%) GII.b/GII.3 (2.4%) GII.5 (2.4%) GII.4/GII.12 (2.4%) Two GII.4 variants identified: 2006a (61.8%) and 2006b (11.3%).		
Mattner, F; 2006 [57]	Prospective controlled study 1,3,4,6,7	To characterize risk factors for the clinical complications of norovirus infections (e.g. vomiting, diarrhea, potassium decrease, creatinine increase, C-reactive protein increase)	All individuals working in or admitted to five wards (psychiatry, nephrology, gastroenterology, cardiology and trauma) at a university hospital in Germany in the period from the onset of clinical symptoms of the first patient until 2 days after the last patient became symptom free. All patients and staff members who were affected with a sudden onset of diarrhea and/or vomiting were included as cases. Patients admitted with clinical signs were regarded as index cases, and patients admitted ≥48 hrs before developing clinical signs were regarded as nosocomial cases 84 patients (72 acquired infection nosocomially) and 79 staff members (60 nurses). 3 norovirus positive patients were excluded from risk factor analysis. N for risk factor analyses was 53 for all outcomes except C reactive protein increase (N=52)	**Clinical features in patients** (study duration 3 months) Diarrhea – 79/84; 95% Vomiting – 57/84; 68% Somnolence – 2/84; 2% Serum creatinine increase > 10% – 22/84; 26% Serum potassium decrease > 20% – 7/84; 8% **Comparisons of attack rates in patients and nurses** (study duration 3 months) *All results are attack rate (%) in patients vs. nurses; P value* Psychaitry ward – 78 vs. 88; <0.01 Nephrology ward – 32% in the first period and 33% in the second period in patients. Data for nurses not given Gastroenterology – 27 vs. 90; <0.01 Cardiology – 42 vs. 44; 0.87 Trauma – 35 vs. 83; <0.01 Total – 38 vs. 76; <0.01 **Risk factors for complications of norovirus** (study duration 3 months) *VOMITING>1 DAY:* *Univariate analysis: All results OR; P value* Age > 65 years – 1.84; 0.30 Male gender – 0.91; 1.00 Underlying cardiovascular disorders – 2.7; 0.13 Underlying gastrointestinal disorders – 0.34; 0.31 Underlying autoimmune disease – 0.81; 1.00 Underlying renal disorders – 0.95; 1.00 Renal transplant – 1.31; 0.75 Underlying malignancy – P value 0.18; OR not reported Underlying trauma – 1.14; 1.00 Immunosuppressive therapy – 0.92; 1.00 Community acquired norovirus – 2.36; 0.19	Diarrhea was defined as three or more episodes of loose stools in a 24 hr period. Cases were considered to be norovirus-positive if samples from at least two patients from the same ward were positive by norovirus-specific RT-PCR. Power and sample size not reported	358_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Multivariate analysis: All results OR (95% CI) Underlying cardiovascular disorders – 7.17(1.59-51.2) Community acquired norovirus – 5.54(1.04-42.8) *DIARRHEA>2 DAYS:* *Univariate analysis: All results OR; P value* Age > 65 years – 3.58; 0.01 Male gender – 2.15; 0.12 Underlying cardiovascular disorders – 2.80; 0.15 Underlying gastrointestinal disorders – 0.22; 0.03 Underlying autoimmune disease – 4.67; 0.24 Underlying renal disorders – 1.77; 0.39 Renal transplant – 1.71; 0.54 Underlying malignancy – 0.07; 0.01 Underlying trauma – 0.27; 0.053 Immunosuppressive therapy – 1.29; 0.79 Community acquired norovirus – 3.09; 0.06 *Multivariate analysis: All results OR (95% CI)* Age > 65 years – 11.56(1.89-224.00) Underlying malignancy – 0.02(0.00-0.19) Underlying trauma – 0.05(0.00-0.55) *POTASSIUM DECREASE >20%:* *Univariate analysis: All results OR; P value* Age > 65 years – 0.94; 1.00 Male gender – 0.90; 1.00 Underlying cardiovascular disorders – 5.17; 0.06 Underlying gastrointestinal disorders – 0.46; 0.67 Underlying autoimmune disease – 0.98; 1.00 Underlying renal disorders – 1.74; 0.71 Renal transplant – 3.91; 0.09 Underlying malignancy – P value 0.58; OR not reported Underlying trauma – P value 0.19; OR not reported Immunosuppressive therapy – 2.83; 0.25 Community acquired norovirus – 0.48; 0.68 *Multivariate analysis: All results OR (95% CI)* Underlying cardiovascular disorders – 17.10(2.17-403.00) Renal transplant – 13.02(1.63-281.00)		

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				CREATININE INCREASE >10%: *Univariate analysis: All results OR; P value* Age > 65 years – 1.04; 1.00 Male gender – 1.79; 0.24 Underlying cardiovascular disorders – 0.60; 0.42 Underlying gastrointestinal disorders – 1.93; 0.36 Underlying autoimmune disease – 4.50; 0.12 Underlying renal disorders – 1.44; 0.59 Renal transplant – 3.53; 0.07 Underlying malignancy – 0.93; 1.00 Underlying trauma – 0.07; <0.01 Immunosuppressive therapy – 5.74; <0.01 Community acquired norovirus – 5.07; 0.01 *Multivariate analysis: All results OR (95% CI)* Immunosuppressive therapy – 5.67(1.78-20.1) *C REACTIVE PROTEIN >58 MG:* *Univariate analysis: All results OR; P value* Age > 65 years – 0.81; 0.79 Male gender – 2.63; 0.11 Underlying cardiovascular disorders – 0.32; 0.06 Underlying gastrointestinal disorders – 1.54; 0.55 Underlying autoimmune disease – 3.71; 0.14 Underlying renal disorders – 2.13; 0.19 Renal transplant – 1.33; 0.76 Underlying malignancy – 2.96; 0.25 Underlying trauma – 0.23; 0.35 Immunosuppressive therapy – 3.38; 0.06 Community acquired norovirus – 2.30; 0.23 *Multivariate analysis: All results OR (95% CI)* Underlying malignancy – 9.07(1.17-193.00) Immunosuppressive therapy – 5.37(1.62-19.9)		
Adamson, WE; 2007 [109] 3,4	Descriptive study	To determine if the increased number of norovirus cases in Scotland during early 2006 was due to the emergence of a new	A representative number of norovirus cases from outbreaks in Scotland were analyzed at the West of Scotland Specialist Virology Centre laboratory	**norovirus GII genotype 4 variants** (study duration 19 months) 1/2005-2/2006 vs 3/2006-8/2006: 69/84 (82%) GII-4 v3 vs 61/77 (79%) GII-4 v4		011_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
		norovirus variant	149 samples were GII genotype 4			
Gallimore, CI; 2004 [110]	Descriptive study 3,4	To determine if norovirus was present during a 2002 outbreak in a pediatric tertiary hospital and determine the strains in symptomatic vs. asymptomatic patients.	Staff and patients in a pediatric tertiary hospital during a norovirus outbreak in June-July 2002. 9 symptomatic (6 patients and 3 staff members). 99 asymptomatic (12 patients and 87 staff members). Point prevalence survey.	**norovirus strains** Symptomatic vs. asymptomatic patients and staff– 9/9 (100%) GII-3a vs 27/99 (27%) GII-4.	Asymptomatic excretion of norovirus can occur. However, in this case, the strain did not cause nosocomial infection and may suggest either low level excretion or commensal carriage	673_IL

Environmental characteristics

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
MMWR; 2008 [79]	Prospective controlled study. 1,3,4	To investigate an outbreak at an elementary school.	Students and staff at an elementary school in Washington DC in February 2007. Students – median age 8 years (range 3-12 years); 55% female. Staff – median age 41 years (range 13-66 years); 92% female. 266 – 207 students and 59 staff.	**Symptomatic norovirus infection** *Bivariate analysis: All results RR (95% CI); p value* Being a student – 0.94 (0.66-1.34); 0.76 Being female – 1.13 (0.82-1.56); 0.52 Having an ill contact – 1.76 (1.16-2.67); 0.01 Classroom J (first) – 1.94 (1.34-2.80); 0.02 Library use: 0.94 (0.58-1.52); 0.87 Library computer use: 1.08 (0.41-2.84); 1.00 **Interventions implemented** District of Columbia Department of Health recommended -more thorough handwashing - cleaning all shared environmental surfaces with a diluted (1:50 concentration) household bleach -cleaning computer equipment (i.e., mice and keyboards) -excluding ill persons from school for at least 72 hours after resolution of illness	A case of gastrointestinal illness was defined as illness in a student or staff member with nausea, vomiting, or diarrhea, who was at the school February 2-18, 2007. Power and sample size not reported.	017_IL
MMWR, 2007 [80]	Prospective controlled study 1,2,3,4	To investigate source of norovirus gastroenteritis outbreak at a family reunion.	Family reunion in Grant county, West Virginia, October 2006. 39 included in cohort study: 19 are cases and 20 are controls.	***Risk factor – unadjusted RR (95% CI); p value*** Food consumed Scalloped potatoes – RR 2.80 (1.14-6.86); 0.01 Ham – RR 2.19 (0.63-7.60); 0.24 Chicken – RR 2.16 (0.97-4.81); 0.04	12/13 stool specimens tested positive for norovirus genogroup II by RT-PCR. Power and sample size not	3864_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Chocolate cheese ball – RR 2.14 (1.26-3.65); 0.04 – only eaten by 7 individuals Onion dip – RR 1.65 (0.88-3.07): 0.23 Meatballs – RR 1.54 (0.79-3.03); 0.21 Green beans – RR 1.44 (0.76-2.73); 0.27 Cream cheese roll-ups – RR 1.43 (0.77-2.65); 0.29 Cheese ball – RR 1.43 (0.72-2.83); 0.66 Chip dip – RR 1.33 (0.69-2.54); 0.42 Buterscotch cake – RR 1.24 (0.61-2.52); 0.71 Cole slaw – RR 1.17 (0.60-2.30); 0.65 Deviled eggs – RR 1.11 (0.59-2.10); 0.75 Pasta salad – RR 1.04 (0.57-1.89); 0.90 Broccoli salad – RR 1.04 (0.52-2.07); 0.92 Chocolate cake – RR 1.03 (0.36-2.94); 1.00 Pinch-me cake – RR 1.03 (0.36-2.92); 1.00 Sugar cookies – RR 1.00 (0.42-2.39); 1.00 Coffee – RR 1.00 (0.46-2.19); 1.00 Soda – RR 0.90 (0.47-1.70); 0.74 Spicy rice casserole – RR 0.89 (0.39-1.77); 1.00 Parsley potatoes – RR 0.83 (0.39-1.77); 0.63 Potato casserole – RR 0.74 (0.37-1.50); 0.40 Raw vegetables – RR 0.74 (0.34-1.62); 0.43 Pecan cake – RR 0.70 (0.27-1.83); 0.69 Coffee creamer – RR 0.69 (0.13-3.54); 1.00 Mandarin orange cake – RR 0.63 (0.19-2.04); 0.66 Macaroni salad – RR 0.53 (0.22-1.28); 0.11 Turkey – RR 0.40 (0.0-2.39); 0.35 Baked beans – RR 0.38 (0.11-1.34); 0.12 Fruit cocktail – N/A Other risk factors Contact with ill person – RR 2.27 (1.01-5.07); 0.03 At home A prereunion gathering – RR 1.57 (0.87-2.81); 0.24 At home B prereunion gathering – RR 0.92 (0.46-1.81); 0.80	reported.	
Costas L, 2007 [81]	Prospective controlled study 1,2,3,4,6,7	To investigate a norovirus outbreak among hospital staff.	Healthcare workers at a hospital in Barcelona, Spain. 31/38 cases available for interview. 31 unmatched healthcare workers selected as controls	***Risk factor – OR (95% CI); p value*** Rice salad with cocktail sauce – OR 4.11 (1.14-14.72); 0.03 Waterborne source – OR 0.675 (0.237-1.924) September 12th (when rice salad with cocktail sauce served) – OR 3.37; p=0.07	norovirus identified from stool samples – testing used not defined. Power and sample size not reported.	IL_6577

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
Lopman, BA; 2005 [82]	Prospective controlled study 1,2,3,4,6,7	To evaluate institutional factors related to gastroenteritis outbreaks in hospitals.	Outbreaks occurring in 3 hospital administrations (NHS trusts) in England. These trusts include 4 major acute hospitals and 11 community hospitals, which comprise 171 inpatient functional care units.	**Outbreak rates** (study duration 52 weeks) *Overall* 227 outbreaks in 113 units – 1.33 outbreaks/unit-year *Hospital Type* Acute center vs. community – 1.5 (1.3-1.8) vs. 0.9 (0.7-1.2); 0.0002 *All results are rate (95% CI)* Unit specialty; p<0.0001 Other types – 1.0 (0.8-1.3) General medical – 2.5 (1.9-3.2) Geriatric – 1.9 (1.4-2.6) Surgical – 1.2 (0.8-1.8) Orthopaedics – 1.9 (1.2-2.9) Mental health – 0.7 (0.3-1.5) No previous outbreak vs. previous outbreak – 0.9 (0.8-1.1) vs. 2.4 (2.0-2.9); p<0.0001 Month following outbreak vs. rest of follow-up period – 3.3 (2.4-4.6) vs. 1.3 (1.1-1.5); p<0.0001 **Outbreak risk factors** (study duration 52 weeks) *All results are HR (95% CI); p value* *Univariate analysis* Number of beds in unit (per additional 10 beds) – 1.50 (1.25-1.81); <0.0001 Average length of stay (per additional week) – 0.96 (0.92-1.00); 0.04 Unit in acute centre vs. community hospital – 1.80 (1.31-2.49); 0.0002 Previous outbreak – 2.00 (1.50-2.67); 0.0001 Month following outbreak vs. other time – 2.05 (1.41-2.98); <0.0001 General medicine vs. geriatric vs. orthopaedics – 2.48 (1.76-3.49) vs. 1.94 (1.32-2.85) vs.1.90 (95% CI 1.17-3.08); <0.0001 *Multivariable analysis* Number of beds in unit (per additional 10 beds) – 1.22 (0.96-1.55); 0.10 Average length of stay (per additional week) – 0.89 (0.80-0.99); 0.041 Previous outbreak – 0.88 (0.62-1.25); 0.47 Hospital ward type – p=0.006	Power and sample size not done. noroviruses were detected in 65% of all outbreaks where specimens were available.	511_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				General medicine – 1.71 (1.11-2.63) Geriatric – 2.55 (1.52-4.25) Surgical – 0.79 (0.48-1.29) Orthopaedics – 1.43 (0.82-2.49) Mental Health – 2.30 (0.36-14.9)		
Evans, M; 2002 [83]	Prospective controlled study 1,3,4	To describe an outbreak of norovirus gastroenteritis following vomiting by an attendee at a concert	Primary school children attending a concert at a metropolitan concert hall. Demographic characteristics not provided. 1229 children from 15 primary schools	**Description of outbreak** Following the vomiting, cleaning was done with an ordinary vacuum cleaner the following day. No hypochlorite based product was used. The index case was seated in tier 13. **Auditorium seating as a risk factor for symptomatic norovirus infection** (follow-up not clearly reported) Children seated in tiers 9-13 vs. children seated elsewhere – 199/387 vs. 58/797; RR(95% CI) = 7.1(5.4-9.2)	A case was defined as a person who had attended the concert hall and had developed vomiting and/or diarrhea within 24-72 hrs of the visit. NLV was confirmed in fecal samples using RT-PCR Power and sample size not reported	897_RA
Lachlan, M; 2002 [84]	Prospective controlled study 1,3,4	To describe an outbreak of norovirus gastroenteritis and lessons learned.	Persons with a connection to a hotel linked to the outbreak or ill contacts of people who were unwell and had a connection with the hotel. 112 potentially exposed, 79 cases	**Symptomatic norovirus infection - Food specific attack rates** Beef sandwich – 1.35(1.08-1.67) Cheese sandwich – 1.33(1.06-1.67) Egg sandwich – 1.49(1.18-1.88) Ham sandwich – 1.39(1.14-1.69) Lamb sandwich – 1.46(1.28-1.66) Tuna sandwich – 1.27(1.02-1.60) Sausage sandwich – 1.01(0.77-1.32) Soup – 1.28(1.00-1.64), P<0.05 Parsley garnish – 0.71(0.18-2.83) Tomato garnish – 1.15(0.82-1.61) Hot chocolate – 1.45(1.28-1.65) Tea – 1.04(0.81-1.33) Coffee – 1.36(1.10-1.67) Ice – 1.25(1.00-1.57) Other drinks – 1.52(1.12-2.05) After applying a critical P value (<0.003) with Bonferroni correction, only egg sandwich and drinks from the bar (other drinks) were found to be statistically significant. **Lessons from the outbreak** 1. Outbreak control team meetings that are formally minuted with	A case was defined as someone with symptoms of diarrhea, vomiting or abdominal pain or any combination of these more than once in 24 hours and a connection with the hotel where the outbreak started. norovirus was confirmed by EM	942_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				action points being highlighted on a flipchart 2. Good liaison with laboratory services to agree on clear pathways for the delivery and analysis of samples that became available during normal working hours or were processed over the weekend. 3. Rapid virological confirmation to reassure the public that appropriate control measures were in place and handle the media interest. 4. Joint visit to the outbreak premises by protective services and public health representatives to facilitate clear and open communication between all parties and secure a voluntary agreement from the hotel owner to cease all food preparation. 5. Food handlers should remain off work from onset of illness until 48 hours after diarrhea and vomiting have ceased 6. All those involved in carrying out interviews and analyzing data working from one site and through one computer network to improve the efficiency of working through contact lists, allowing rapid assessment of the epidemic curve and symptom pattern and the results of RR calculations of the foodstuffs.		
Love, S; 2002 [85]	Prospective controlled study 1,3,4	To describe an outbreak of gastroenteritis and procedures implemented to control it.	Guests and employees of a Virginia hotel. There were 3 groups: Group A: Attendees of a business conference (n=110); median age of cases (n=34) 52 years; 59% cases female Group B: Physicians and their families (n=95); median age of cases (n=11) 31 years; 73% cases female Group C: Retired persons (n=310); median age of cases (n=15) 71 years; 60% cases female 60 cases	**Risk factors for symptomatic norovirus infection** (follow-up unclear) Attending reception: RR(95% CI) – 2.1(1.1-4.0) Eating coleslaw at picnic: RR(95% CI) – 3.6(1.0-13.6) **Interventions** Infection control measures instituted: 1. Employees who were ill in the past two weeks or had an ill child in diapers were excluded from work for 1 day. Employees who were currently ill with vomiting or diarrhea were told not to work for 1 day after resolution of symptoms 2. All employees were instructed about hygiene and hand washing 5 days after initial cases 3. The facility was closed for 8 h to permit thorough cleaning of all food service areas and guest rooms. New guests were not accepted until all guestrooms, bathrooms, and common rooms were thoroughly cleaned 7 days after initial cases 4. All cold food requiring hand-preparation was excluded from the menu. No open bowls of food such as chips or popcorn were served 7 days after initial cases **Response to intervention** (at two week follow-up) The hotel reported no further ill guests or employees	A case was defined as vomiting or diarrhea in a hotel attendee or staff. norovirus confirmed by RT-PCR Power and sample size not reported.	915_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
Anderson, AD; 2001 [86]	Prospective controlled study 1,3,4	To identify the source of a gastroenteritis outbreak at a car dealership.	Multistate investigation involving catered meals given to car dealerships spanning 13 states. Median age 37 years (range 3-89 years). 753 banquet attendees. 333 met case definition.	**Symptomatic norovirus infection** *Univariate analysis* *All results are RR (95% CI)* Any salad – 3.8 (2.5-5.6) Rotini pasta salad – 3.0 (2.4-3.7) Potato salad –1.6 (1.3-1.9) Bow-tie pasta salad –1.5 (1.3-1.8) Vegetable salad – 1.7 (1.4-1.9) Condiments – 1.4 (1.2-1.7) Dips – 1.3 (1.1-1.5) Cheeses – 1.3 (1.1-1.5) Snacks –1.0 (0.8-1.1) Meats – 1.1 (0.7-2.0) Desserts – 1.2 (1.0-1.4) Breads – 1.4 (1.1-1.9)	Case was a person who attended a "banquet dinner" at one of the dealerships and developed vomiting or diarrhea (≥3 loose stools within 24 hours). 2/15 caterers had elevated norovirus immunoglobulins. 16 specimens that were sequenced showed a common outbreak strain. Power and sample size not reported.	1003_IL
Cunney RJ, 2000 [87]	Prospective controlled study 1,2,3,4	To investigate a hospital NLV outbreak.	Hospital outbreak N= 95 persons: 47 patients and 48 staff.	**Infection control practices** -Affected patients were cohorted -Admissions to and transfers from the geriatric ward were stopped -70% alcohol hand rub supplemented routine hand washing -Affected staff sent home until 48 hours after symptoms subsided -Decontamination procedures changed from standard phenolic solution to 2% hypochlorite solution **Food source** Drinking water from the hospital water supply: 16 symptomatic and 6 nonsymptomatic (p=0.1)	12 (13%) containing SRSV were solid phase immune electron microscopy (SPIEM) positive for NLV 25 (27%) sampes contained small round featureless virus (SRFV) identified by direct EM and were negative on SPIEM Power and sample size not reported.	1197_IL
Marks, P; 2000 [88]	Prospective controlled study 1,3,4	To describe an outbreak of gastroenteritis following a meal in a hotel during which one of the diners	Diners attending an evening dinner at a large hotel in the UK. Demographic characteristics not reported	**Symptoms** (% of ill subjects reporting symptoms) Nausea – 58 Diarrhea and vomiting – 42 Vomiting without diarrhea – 21 Diarrhea without vomiting – 21	NLV was confirmed using EM and RT-PCR 83 of 126 guests (66%) returned completed	1122_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
		vomited	126; 52 cases	Abdominal pain – 40 Fever – 38 **Time of onset of symptoms** 83% of those who became ill did so between 13 and 48 hours after the meal and 59% between 25 and 48 hours. Of the 14 people who reported precise times for the onset of their illness, the mean time from exposure to onset of symptoms was 33 hours and the median 35 hours. **Symptomatic norovirus infection - Attack rate in %** (at each of the tables) The lady who vomited was seated at table 2 Table 1 – 71 Table 2 – 91 Table 3 – 56 Table 4 – 50 Table 5 – 40 Table 6 – 25 There was a signifiant relationship between distance from the vomiter and the risk of becoming ill (P<0.01) with no significant deviation from that trend (P=0.68)	questionnaires Power and sample size not reported	
Lo SV, 1994 [89]	Prospective controlled study 1,2,3,4	To investigate a SRSV gastroenteritis outbeak in 4 hospitals served by one central kitchen.	4 hospitals - 1 acute district general hospital and 3 smaller peripheral hospitals with long-stay and rehabilitation patients 81 patients and 114 staff in 4 hospitals Buffet lunch cohort study: N=41 completed quesionnaire Patient case-control study: N= 23/24 cases and 35/36 controls completed questionnaires. Staff case-control study: N= 22/27 cases and 49/54 controls completed questionnaire.	***Buffet lunch study*** ***Food - RR (95% CI)*** Ham and tomato – RR 1.0 (0.6-1.7) Cheese and pickle – RR 0.8 (0.4-1.9) Turkey salad – RR 2.4 (1.4-4.1) Tuna – RR 1.2 (0.7-2.0) Sausage roll – RR 1.1 (0.6-1.8) Cheese and pineapple – RR 1.0 (0.6-1.8) Sausage mushroom – RR 1.6 (0.-2.9) Fresh fruit – RR 0.8 (0.3-2.3) Meringue – RR 0.9 (0.5-1.4) Orange juice – 1.0 (0.48-2.0) Wine – 1.0 (0.51-2.1) ***Patient case-control study*** ***Risk factor*** ***Food - OR (95% CI)*** March 7th Beel cobble – OR 0 (0-1.7)	A cohort study of staff who attended a retirement buffet lunch, a patient case-control study based at the district general hospital, and a nursing staff case-control study at the district general hospital were performed. Fecal samples underwent bacteriological examination, routine EM, and immuno-EM. Power and sample size not reported.	1540_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Beef crumble – OR 1.6 (0-11.5) Mince – OR 0.7 (0.1-3.9) Sausage and onion – OR 0.3 (0.1-1.3) Cheese pie – OR 0.2 (0-1.6) Lamb salad – OR 0.4 (0.05-2.4) Tuna salad – OR 6.6 (1.0-71.6); p<0.05 Any salad – OR 1.8 (0.5-6.8) Corn beef sandwich – OR 1.6 (0.1-23) Any sandwich OR 4.6 (0.6-39) March 8th Cod – OR 1 (0.3-3.5) Chicken curry – OR 0.8 (0.2-2.8) Flaked fish – OR 0.7 (0.01-15) Lamb casserole – OR 0.9 (0.2-3.9) Mushroom pizza – OR 0.3 (0.01-3.9) Savoury lamb – OR 1 (0.1-9.7) Beef salad – OR 3.2 (0.2-97) Chicken salad – OR 2.5 (0.3-31) Any salad – OR 4.7 (0.9-30); p <0.05 Salmon sandwich – OR 0.2 (0-2.2) Any sandwich – OR 0.4 (0.04-2.3) March 9th Pork casserole - OR 1.5 (0.4-5.7) Chicken pie – OR 0.3 (0.1-1.5) Minced chicken – OR 0.2 (0-1.6) Cawl – OR 1.6 (0.2-13) Fishcake – OR 0.5 (0.1-2.5) Egg salad – OR 0.3 (0-3.9) Cheese salad – OR 2.2 (0.2-4.8) Any salad – OR 1.1 (0.2-4.8) Ham sandwich – OR 0.5 (0.01-6.7) Any sandwich – OR 1 (0.1-9.7) ***Staff case-control study*** No statistically significant associations found. 1 food handler who prepared the salad had a child who was ill 2 days prior and the food handler became ill the day following food preparation. ***Infection control practices*** Closure of the central kitchen		

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Disposal of all remaining food Discontinuing all hospital admissions and ward transfers Daily ward cleaning with 2% hypochlorite Emphasis on hand washing		
Patterson T, 1993 [90]	Prospective controlled study 1,2,3,4,67	To investigate an SRSV gastroenteritis outbreak at a conference.	Outbreak at an international AIDS conference. April 23, 1990. N=226/283 (80%) delegates replied to the questionnaire.	***Risk factor – Unadjusted RR (95% CI); p value – the foods prepared by potential source (foodhandler) italicized*** Wednesday, April 18, 1990 Canapes – RR 1.21 (0.80-1.84); 0.44 *Celery – RR 1.16 (0.76-1.79); 0.59* Sausage – RR 1.2 (1.01-2.30); 0.07 Thursday, April 19, 1990 buffet Chicken drumsticks – RR 1.66 (1.08-2.55); 0.03 Green salad – RR 1.42 (0.87-2.31); 0.20 Tomato and chive salad – RR 0.79 (0.51-1.23); 0.36 *Ham – RR 2.18 (1.38-3.44); <0.001* Vegetable pie – RR 0.76 (0.46-1.25); 0.34 Coleslaw – RR 0.84 (0.52-1.37); 0.59 *Coleslaw and rice – RR 1.27 (0.80-2.02); 0.38* Thursday, April 19, 1990 civic reception *Melon – RR 1.19 (0.78-1.82); 0.51* *Sole – RR 1.12 (0.73-1.70); 0.70* *Lamb – RR 1.23 (0.80-1.89); 0.42* Vegetables – RR 1.31 (0.85-2.01); 0.28 *Chocolate roulade – RR 0.97 (0.64-1.48) 0.98* Cheese – RR 1.04 (0.67-1.63) Friday, April 20, 1990 buffet *Coronation chicken – RR 3.51 (2.23-5.52); <0.0001* Green salad – RR 1.78 (1.12-2.84); 0.018 Vegetable quiche – RR 1.07 (0.70-1.63); 0.88 *Potato salad – RR 1.45 (0.95-2.21); 0.11* Curried rice – RR 1.43 (0.93-2.19); 0.13 Tomato and chive salad – RR 1.02 (0.73-1.43); 0.99 Chicken and ham pie – RR 1.25 (0.80-1.96); 0.43 Coleslaw – RR 1.13 (0.48-2.66); 0.76 Highest attack rates for coronation chicken and ham prepared by suspected source (foodhandler). Adjusted analyses found only cornocation chicken was associated with illness: *Coronation chicken – RR 3 (1.9-4.8); <0.0001*	SRSV visualized on EM in 2/5 samples. A member of the catering staff attended a children's party April 15th where there was a child with gastrointestinal illness.April 17th the staff member had vomiting and diarrhea, came to work, and was sent home. She returned on April 19th asymptomatic and helped prepare meals for the conference. Power and sample size not reported.	1625_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
Alexander WJ, 1986 [91]	Prospective controlled study 1,2,3,4	To investigate a norovirus outbreak at a college campus.	College campus in Jefferson County, Alabama in November 1981 N=92	**Patient-control analysis of foods eaten and development of illness (Meal: Item – No. of discardant pairs (patients vs. controls); p value** Noon, Nov 15th: fried chicken – 2 vs. 4; NS Noon, Nov 16th: chicken/dumplings – 2 vs. 8; NS Noon, Nov 16th: corn – 6 vs. 3; NS Noon, Nov 16th: BBQ beef – 3 vs. 0; NS Noon, Nov 16th: lettuce – 11 vs. 2; 0.02<p<0.05 Evening, Nov 16th: lettuce - 7 vs. 1; NS Noon, Nov 17th: mashed potatoes - 4 vs. 1; NS Noon, Nov 17th: lettuce – 8 vs. 4; NS Evening, Nov 17th: lettuce – 9 vs. 2; NS	Serologic evidence of Norwalk virus infection. Power and sample size not reported.	1935_IL
de Wit, M; 2007 [92]	Retrospective controlled study 1,3,4,6,7	To describe an outbreak of gastroenteritis caused by a baker infected with norovirus who continued to work in his bakery having washed his hands and disinfected countertops.	Staff of a department in the Netherlands who attended a reception where the outbreak was reported. Median age 39 years; 45% female. 800-900 employees; 231 reported diarrhea or vomiting	**Symptoms** Diarrhea and vomiting – 76% Diarrhea only – 12% Vomiting only – 12% Median time to onset of symptoms – 31 hours **Symptomatic norovirus infection** *All results OR(95% CI)* *Univariate analysis* Coffee – 0.3(0.1-0.9) Tea – 0.7(0.2-2.0) Milk – 1.3(0.9-1.9) Butter milk – 1.1(0.7-1.8) Orange juice – 1.2(0.8-1.6) Champagne – 1.6(1.1-2.3) Cheese – 1.5(1.1-2.2) Brie – 1.1(0.7-1.8) Ham – 1.5(1.0-2.2) Beef – 1.2(0.8-1.9) Tuna salad – 1.6(1.1-2.4) Salmon salad – 2.2(1.0-4.5) Egg salad – 1.4(0.9-2.1) Raisin roll – 0.9(0.6-1.3) Increasing number of rolls – 2.0(1.6-2.4) *Multivariate analysis* Coffee – 0.4(0.1-0.8) Raisin roll – 0.5(0.3-0.8) Number of rolls – 2.0(1.5-2.5)	A case was defined as a member of the departmental staff who attended the reception and reported diarrhea (3 or more loose stools a day) or vomiting in the 72 hours following the reception. A control was defined as a member of the department staff attending the reception without diarrhea or vomiting in the 72 hours following the reception. norovirus infection was confirmed using RT-PCR The estimated response rate for questionnaires among cases was nearly 100%. The estimated response rate among controls was 40-50% Power and sample size not reported	4084_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Intervention implemented Sick food handlers excluded from work for 48hrs and reinforcement of hygiene measures		
MMWR; 2007 [93]	Retrospective controlled study 1,2,3,4	To identify the source of a restaurant outbreak.	Subjects who ate at a Michigan restaurant in January/February 2006 during a norovirus outbreak. Cases – median age 40 years (range 1-92 years); 58.5% female. 364 patrons met case definition for the descriptive study. The case control study included 45 cases and 91 controls.	**Symptomatic norovirus infection** *All results in OR (95% CI)* Antipasti platter – 2.96 (1.08-8.14) Garlic mashed potatoes – 4.05 (1.37-11.99) Several food service workers reported to work ill including one line cook who vomited at the work station. **Interventions:** -Food prepared during January 27-30th was discarded -Ill employees were excluded from work for at least 72 hours after symptoms had subsided. -Facility was cleaned extensively.	Case for the descriptive study was a patron who had eaten food at the restaurant between January 19-February 3, 2006 and developed vomiting or diarrhea within 10-50 hours. A case for the employee was an employee with vomiting or diarrhea during that time period. For the analytic study, case patron was someone who had eaten at the restaurant from January 28-29 and developed vomiting or diarrhea 10-50 hours after eating. A control was a patron with the same exposure but no gastrointestinal illness. Power and sample size not reported.	046_IL
Rizzo C, 2007 [94]	Retrospective controlled study 1,2,3,4,6,7	To investigate risk factors for a norovirus outbreak in a resort.	Resort in Puglia region of Italy during a three week period in July 2005. 400 guests during outbreak 150 guests available at the start of investigation and 41 (27.3%) cases identified. N= 41 cases and 41 matched controls.	***Risk factor – cases # (%) vs. controls # (%): OR (95% CI); p value*** ***Only variables included in conditional logistic model have multivariate OR listed*** Ice – 21 (51%) vs. 12 (29%): univariate OR 4.1 (0.9-7.1); 0.04 multivariate OR 16.4 (1.8-250.9); 0.04 Eggs – 2 (5%) vs. 8 (19%): univariate OR 2.3 (0.1-1.7); 0.12 Grilled sausage – 21 (51%) vs. 25 (61%): univariate OR 0.7 (0.2-1.7); 0.17 Ham – 1 (2%) vs. 5 (12%): univariate OR 2.8 (0.1-1.7); 0.09 Grilled meat – 11 (27%) vs. 15 (37%): univariate OR 3.5 (0.1-1.1); 0.06 Snacks – 20 (49%) vs. 19 (46%): univariate OR 0.1 (0.4-2.8); 0.15 Raw mussels – 22 (54%) vs. 13 (31%): univariate OR 3.9 (0.9-6.8); 0.04 multivariate OR 25.5 (1.5-442.9); =0.03	18/20 (90%) fecal samples were positive for norovirus by RT-PCR 3 samples confirmed GGII norovirus. One matched control was selected for each case assuming 25% exposed controls, 80% power to detect OR 4.1, alpha error of 5%.	3_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
Schmid, D; 2007 [95]	Retrospective controlled study 1,3,4,6,7	To identify the source of a norovirus outbreak at a telephone company.	Cases were employees or external persons who ate lunch at the canteen of the telephone company in Austria and developed gastroenteritis. 325	**Symptomatic norovirus infection - Attack rate** 182/325 (56%) **Symptomatic norovirus infection** *Demographic characteristics* Age – cases 38.4 years (SD 11.33) vs controls 34.5 years (SD 12.7); p=0.004 Female – RR 1.23 (95% CI 1.02-1.5); p=0.054 *Working days* *Univariate analysis: All results RR (95% CI); p value* Monday – 0.06 (0.02-0.2) Tuesday – N/A Wednesday – 18.82 (11.82-29.96); <0.001 Thursday – 2.14 (1.65-2.79); <0.001 *Multivariate analysis: All results RR (95% CI)* Monday – 0.08 (0.02-0.25) Tuesday – N/A Wednesday – 3.05 (2.18-4.28) Thursday – 1.89 (1.27-2.81) *Day-by-day food specific analysis* *Univariate analysis: All results RR (95% CI)* Monday salad – N/A Monday potatoes – 0.94 (0.09-10.17) Tuesday potatoes – 0.66 (0.39-1.14) Tuesday compote – 1.40 (0.77-2.54) Tuesday salad – 2.51 (0.61-10.31) Wednesday rice with beans –1.39 (1.04-1.85) Wednesday salad – 3.44 (1.24-9.59) Thursday semolina dumpling soup – 2.94 (1.57-5.52) Thursday roast pork –1.72 (0.96-3.07) Thur sday potatoes –1.37 (0.81-2.32) Thursday sauerkraut –1.86 (1.06-3.26) Thursday salad – 1.04 (0.64-1.7) *Multivariate analysis: All results RR (95% CI); p value*	Gastroenteritis was defined as someone with symptoms of diarrhea (≥3 stools in 24 hours) and/or projectile vomiting after January 15, 2006. Power and sample size not reported. Most likely source of outbreak was a kitchen assistant who prepared the salad.	031_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Monday salad – N/A Monday potatoes – 0.78 (0.05-13.67); 0.87 Tuesday potatoes – 0.80 (0.37-1.71); 0.57 Tuesday compote – 1.11 (0.50-2.43); 0.80 Tuesday salad – 2.19 (0.73-6.52); 0.16 Wednesday rice with beans –1.24 (0.96-1.61); 0.1 Wednesday salad – 2.82 (1.00-7.94); 0.05 Thursday semolina dumpling soup – 2.53 (1.32-4.83); 0.01 Thursday roast pork – 1.46 (0.55-3.88); 0.45 Thursday potatoes – 0.51 (0.29-0.92); 0.02 Thursday: sauerkraut – 1.91 (0.78-4.68); 0.16 Thursday salad – 1.77 (1.17-2.69); 0.01 **Interventions implemented** Closure of kitchen		
Payne, J; 2006 [207]	Retrospective controlled study 1,3,4	To summarize an outbreak investigation into three norovirus outbreaks and a cluster of community cases. The primary outcome was identifying the source of norovirus illness.	Cases of norovirus outbreak associated with a national submarine sandwich franchise restaurant in Michigan. The 3 outbreaks were at a school staff luncheon, publishing company staff luncheon and a social service organization luncheon. Community cases were also reported. 170 cases	**Symptomatic norovirus infection** School staff luncheon – 23/29; 80% Publishing company staff luncheon – 55/95; 58% Social service organization luncheon – 9/18; 50% Community cases – 25/28; 90% **Predominant symptoms** School staff luncheon – diarrhea (87%) and vomiting (74%) Publishing company staff luncheon – diarrhea (94%) and vomiting (83%) Social service organization luncheon – diarrhea (78%) and vomiting (78%) Community cases – diarrhea (92%) and vomiting (80%) **Source of symptomatic norovirus infection** School staff luncheon – 22/23 cases reported eating lettuce; no specific food item was significantly associated with the illness Publishing company staff luncheon – lettuce – 11.24(1.30-95.2); jalapeno peppers – 3.45(1.04-11.40); onions – 3.09(1.27-7.80) Social service organization luncheon – no specific food item was significantly associated with the illness Community cases – no specific food item was significantly associated with the illness A food handler employed by the restaurant was identified as the source of illness. He had returned to work within a few hours of having symptoms of gastrointestinal illness while he was still excreting norovirus	A case was defined as illness in a person who ate the suspect meal during the outbreak and became ill 8-56 hrs later with vomiting or diarrhea and two of the following: documented fever, abdominal cramps or nausea Cases were identified when the county health department was notified of the outbreak. Power and sample size not reported	326_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				in the stools and lettuce was sliced each morning by him.		
Fretz, R; 2005 [77]	Retrospective controlled study 1,2,3,6,7	To identify risk factors for sporadic norovirus infections.	All patients of general practitioners in German-speaking parts of Switzerland. Cases (mean age 32.7 years; median age 34 years; range 1.1-69.3 years) were subjects who resided in the study area who had an episode of diarrhea and/or vomiting, consulted a practitioner in the study area, had stool samples negative for *Campylobacter, Shigella, Salmonella*, and other gastroenteric pathogens, had stool samples positive for norovirus genogroup I or II. Cases excluded subjects <6 months or >75 years, patients with possible nosocomial disease, and patients who were part of a norovirus outbreak. Controls (mean age 33.2 years; median age 37.1 years; range 1.3-70.1 years) were identified through each patient, were the same sex and age group (defined as 5 year intervals over 5-20 years and 10 year intervals over 20-60 years), lived within 10 km of the case, and had not consulted a general practitioner for gastrointestinal illness or symptoms in the month prior to the questionnaire. 126 cases met study inclusion criteria. 73 matched case-control pairs.	**Symptoms** (study duration 2 years) Diarrhea – 124/126 (98.4%). Vomiting – 84/126 (66.7%). Nausea – 85/126 (67.5%) Fever – 57/126 (45.2%) Headache – 45/126 (35.7%) Abdominal cramps – 87 (69%) Other – 46 (36.5%) **Mean duration of symptomatic illness** 7.3 days (SD, 6.2 days; range 0.25-28 days) **Symptomatic norovirus infection** *Multivariable analysis* *Consumption of food and beverages OR (95% CI); p value* Mineral water – 1.00 (0.46-2.16); 1.00 Salad – 1.25 (0.34-2.65); 0.74 Raw berries – 0.75 (0.17-3.35); 0.71 Tap water – 1.33 (0.56-3.16); 0.51 Sweet beverages – 1.06 (0.55-2.05); 0.87 *Personal contacts OR (95% CI); p value* Household with children ≤2 years) – 1.00 (0.29-3.45); 1.00 Household with children ≤ 5 years – 0.75 (0.26-2.16); 0.59 Household with children ≤ 10 years – 0.75 (0.26-2.16): 0.59 Household with children ≤ 65 years – 0.75 (0.17-3.35); 0.71 Household with children > 1 person – 1.50 (0.53-4.21); 0.44 Household with children > 2 person – 0.77 (0.34-1.75); 0.53 Household with children > 3 person – 0.71 (0.32-1.61); 0.53 Household with children > 4 person – 1.14 (0.41-3.15); 0.53 **Symptomatic norovirus infection** *ABO histo-blood group OR (95% CI); p value - conditional logistic regression* Type A: 1.34 (0.55-3.42); 0.49 Type B: 0.33 (0.07-1.65); 0.15 Type O: 1.00 (0.40-2.52); 0.49 Type AB: 1.50 (0.25-8.98); 0.65 Type A/AB: 1.44 (0.62-3.38); 0.39	Power and sample size reported as 70 matched case-control pairs to detect an OR of 2.9 (alpha 0.05; power 0.80; 0.5 probability of an event in the exposed group). Period between the start of symptoms and completion of the patient questionnaire averaged 29 days (median 24 days).	506_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Type B/AB: 0.63 (0.20-1.91); 0.40 **Symptomatic norovirus infection** *ABO histo-blood group OR (95% CI)*; p value – *random effects logistic regression* Type A: 1.20 (0.55-2.61); 0.64 Type B: 0.28 (0.07-1.13); 0.07 Type O: 1.11 (0.51-2.45); 0.79 Type AB: 1.89 (0.35-10.2); 0.46 Type A/AB: 1.39 (0.64-3.00); 0.40 Type B/AB: 0.59 (0.21-1.70); 0.32		
Grotto, I; 2004 [97]	Retrospective controlled study	To investigate an outbreak on an Israeli military base. 1,3,4	Soldiers at Israel Defense Force training center. 159: 84 males and 75 females. 40 cases and 44 controls for the case control study.	**Risk factor of meals, selected food items, and dining facilities:** *All results – OR (95% CI)* Breakfast Dec 20, 1999 – 1.68 (0.55-5.20) Fresh vegetable salad that meal – 2.62 (0.99-6.96) Lunch Dec 20, 1999 – 4.11 (0.96-24.52) Fresh vegetable salad that meal – 4.38 (1.51-13.35) Dinner Dec 20, 1999 – 0.59 (0.05-5.45) Breakfast Dec 21, 1999 – 1.29 (0.49-3.43) Vegetable salad at that meal – 2.86 (1.05-7.88) Lunch Dec 21, 1999 – 0.70 (0.25-1.91) Dinner Dec 21, 1999 – 0.15 (0.05-0.44) Restaurant – 0.34 (0.13-0.92) Eating at least one meal at a restaurant located off base on Dec 20-21 – 0.34 (0.13-0.92) One food handler was reported being ill and vomiting 2 days before the outbreak. This food handler was not excluded from work and was not present during the iinvestigation.	Cases were defined as any base personnel who during the week of December 19-26, 1999 suffered diarrhea (3 or more loose stools in 24 hours), vomiting or abdominal pain, with or without fever (>37.5 degrees Celsius).	576_IL
de Wit, M; 2003 [61]	Retrospective controlled study (nested case-control study) 1,3,4,6,7	To identify risk factors for norovirus infection	Patients registered at a general practice network in Netherlands. Cases were those persons identified in the community cohort with gastroenteritis and a matched control was selected from the cohort members without gastroenteritis at that time. Median age of case patients was 2 years. Other demographic characteristics were not reported.	**Symptomatic norovirus infection** *All results OR(95% CI) unless otherwise noted* *All case-control pairs* *Univariate analysis* Poor food-handling hygiene (as a score) – 1.3(1.0-1.5); P<0.05 Low education level vs. intermediate education level – 1.9(0.9-4.0) High education level vs. intermediate education level – 2.2(1.2-3.9) Participant to day care center – 1.7(0.9-3.3) Household member to daycare center – 2.0(1.0-3.9) Household member to primary school – 1.6(1.0-2.7) Pets in household – 0.6(0.4-1.0)	Samples were tested for norovirus by RT-PCR Cases and controls were matched by age, degree of urbanization, region and date of inclusion Selection of variables into the multivariable model was backwards manually, based on the log likelihood ratio; a	763_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			152 case-control pairs	Cat as pet – 0.6(0.4-1.0) 1 household member with gastroenteritis vs. none – 3.7(1.7-8.0) >1 household member with gastroenteritis vs. none – 13.1(3.9-34.7) Child household contact – 5.2(1.8-15.3) Adult household contact – 4.4(2.0-9.6) Contact with person outside household with gastroenteritis – 11.4(4.7-27.3) Consumption of fish in the week before onset of symptoms – 1.8(1.0-3.2) Consumption of barbecued food in the week before onset of symptoms – 0.2(0.05-1.0) *Multivariate analysis* Poor food-handling hygiene (as a score) – 1.3(1.0-1.7); P<0.05 1 household member with gastroenteritis vs. none – 1.2(0.3-4.2) >1 household member with gastroenteritis vs. none – 10.9(2.0-60.5) Contact with person outside household with gastroenteritis – 12.7(3.1-51.8) *Population attributable risk (%) (based on multivariate odds ratios)* Poor food handling hygiene – 47 Number of household members with gastroenteritis – 17 Contact with person outside household with gastroenteritis – 56 *<1 year to 4 years (105 case-control pairs)* *Univariate analysis* Poor food-handling hygiene (as a score) – 1.2(0.9-1.5) ≥ 1 household members with gastroenteritis – 4.4(2.2-9.2) Contact with person outside household with gastroenteritis – 17.7(5.1-61.1) *Multivariate analysis* Poor food-handling hygiene (as a score) – 1.2(0.9-1.7) ≥ 1 household members with gastroenteritis – 2.7(0.8-8.9) Contact with person outside household with gastroenteritis – 10.9(2.2-54.6) *Population attributable risk (%) (based on multivariate odds ratios)* Poor food-handling hygiene (as a score) – 46 ≥ 1 household members with gastroenteritis – 27 Contact with person outside household with gastroenteritis – 51	significance level of 0.05 was used. Food handling hygiene was determined using a questionnaire that included items on acquisition and preparation of food. Power and sample size not reported	

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				≥ 5 years (46 case-control pairs) *Univariate analysis* Poor food-handling hygiene (as a score) – 1.3(0.9-1.9) ≥ 1 household members with gastroenteritis – 15.0(2.0-113.6) Contact with person outside household with gastroenteritis – 5.9(1.7-20.1) *Multivariate analysis* Poor food-handling hygiene (as a score) – 1.3(0.8-2.2) ≥ 1 household members with gastroenteritis – 1.1(0.1-15.9) Contact with person outside household with gastroenteritis – 12.1(1.0-147.3) *Population attributable risk (%) (based on multivariate odds ratios)* Poor food-handling hygiene (as a score) – 63 ≥ 1 household members with gastroenteritis – 4 Contact with person outside household with gastroenteritis – 60		
Marks, P; 2003 [98]	Retrospective controlled study 1,3,4,6,7	To describe an outbreak of NLV gastroenteritis during which vomiting occurred in some, but not all, classrooms and thus investigate the importance of vomiting as a mode of transmission of NLV, and the likelihood that environmental contamination played a role in the spread of the outbreak.	Children in a primary school and nursery in the UK. Age range 4-11 yrs. 492	**Symptomatic norovirus infection – Attack rates** (during the study period) *Based on sex [All results % (95% CI)]* Male – 30.4(25.1-36.2) Female – 31.3(25.7-37.6) *Based on age group [All results % (95% CI)]* 3-<4 yr – 20.0(9.5-37.3) 4-<5 yr – 25.9(16.3-38.4) 5-<6 yr – 44.8(32.7-57.5) 6-<7 yr – 52.3(37.9-66.2) 7-<8 yr – 39.0(27.6-51.7) 8-<9 yr – 28.3(18.5-40.8) 9-<10 yr – 27.0(18.2-38.1) 10-<11 yr – 22.2(13.7-33.9) 11-<12 yr – 16.7(8.3-30.6) *Vomiting episodes within classrooms as a risk factor [All results OR(95% CI) unless otherwise noted]* Attack rates increased with the number of vomiting episodes to which pupils were exposed (Chi-squared for linear trend – 37.8; P<0.01) 1 episode vs. none – Unadjusted: 2.7(1.6-4.5); Adjusted*: 5.1(2.2-11.6) 2 episodes vs. none – Unadjusted: 3.0(1.5-5.8); Adjusted*: 3.9(1.8-8.6)	Cases were defined as follows: • for those pupils who returned a questionnaire: those who reported either diarrhea or vomiting or both • for those pupils who did not return a questionnaire: those who were absent from school with symptoms compatible with NLV infection Secondary cases were defined as other household members reporting by questionanaire diarrhea or vomiting after a pupil had been ill. Airborne transmission is implicated but in the	798_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				3 episodes vs. none – Unadjusted: 10.4(4.8-22.4); Adjusted*: 14.6(5.9-36.5) *Exposure to another child vomiting as a risk factor [All results OR(95% CI)]* Unadjusted: 3.9(2.2-7.0); Adjusted*: 4.1(1.8-9.3) **Median time from exposure to onset of illness in days**(during the study period) 3 pupils vomiting on the same day vs. vomiting occurring only once – 1 vs. 14; P<0.01 **Symptomatic norovirus infection - Secondary attack rates** (during the study period) Adults – 17% Children – 46% Overall – 30% (*Adjusted for sex, age and building in which the classroom was situated)	discussion the authors state that aerosolization (eg droplets) from vomiting children may be the method of transmission. Outbreak was confirmed using EIA or PCR for selected specimens Completed questionnaires were returned for 289 pupils (response rate 59%) Study period was 25 June to 16 July 2001 Power and sample size not reported	
Stegenga, J.; 2002 [99]	Retrospective controlled study 1,3,4	To examine the relationship between nurse staffing levels and the rate of nosocomial viral gastrointestinal infections in a general pediatrics population	Patients on a general pediatrics ward in Toronto, Canada. Demographic characteristics not provided. 37	**Symptomatic norovirus infection** *All results Pearson correlation coefficient with norovirus gastroenteritis, P value* Monthly night patient-to-nurse ratio – 0.56; <0.05 Monthly day patient-to-nurse ratio – 0.50; <0.05 Monthly patient census – 0.51; <0.05 Monthly nursing hours per patient day: – 0.38; 0.14 **Symptomatic norovirus infection at 72 hours** *(infections per 1000 patient days)* Nursing hours/patient-day<10.5 vs. >10.5 – 6.39 vs. 2.17; RR(95% CI) = 2.94(2.16-4.01) *All results preinfection period vs. non-preinfection period; P value* **Mean nursing hours per patient day** 12.5 vs. 13.0; <0.05 **Mean nursing hours worked per patient day** 390 vs. 376; <0.01 **Mean patient census** 31.7 vs. 29.5; <0.01	norovirus gastroenteritis was defined according to CDC definition Analysis was done under the assumption of a 72 hr incubation period for norovirus gastroenteritis. The cut-off point for 10.5 nursing hrs per patient day was chosen because the authors deemed this to represent a level of staffing that was inappropriately low, but occurred frequently enough to provide a comparison with more appropriate staffing levels. The 72 hour period prior to each infection was	963_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Day patient-to-nurse ratio 3.31 vs. 3.32; P>0.05 **Night patient-to-nurse ratio** 3.26 vs. 3.16; P<0.05	considered as pre-infection period and all other periods were considered post-infection. Overall, 92 days were defined as pre-infection period and 363 days were defined as non pre-infection period. Power and sample size not reported	
Gotz, H; 2001 [62]	Retrospective controlled study 1,3,4	To describe an outbreak in which secondary transmission into households by individuals occurred	Children and staff at 30 child centers (either a day care facility for preschool children or an after-school center for young children) in Sweden and their household contacts. Child center cases – 79 adults (mean age 41 yrs) and 114 children (mean age 5 yrs) Household cases – 58 adults (mean age 36 yrs) and 21 children (mean age 7 yrs) 775	**Symptoms** *All results adults vs. children - % reporting symptoms; P value* Diarrhea – 71.5 vs. 52.0; <0.01 Vomiting – 64.1 vs. 80.6; <0.01 Nausea – 96.8 vs. 93.1; 0.22 Stomach pain – 87.7 vs. 88.7; 0.82 Headache – 63.6 vs. 43.5; 0.01 Chills – 44.3 vs. 20.8; <0.01 Fever – 44.7 vs. 35.2; 0.20 Myalgia – 48.2 vs. 17.5; <0.01 **Symptomatic norovirus infection - Primary attack rate** Adults vs. children – 68/127 vs. 74/386; P<0.01 Children 0-5 yrs old vs. 6-10 yrs old – 44/204 vs. 30/179; P=0.23 **Symptomatic norovirus infection - Secondary attack rate** Adults vs. children – 11/59 vs. 40/312; P=0.23 Children 0-5 yrs old vs. 6-10 yrs old – 27/160 vs. 12/149; P=0.02 **Risk factors for household transmission of symptomatic norovirus infection** *All results RR(95% CI) unless otherwise noted* Children (vs. adults) – 3.8(1.9-7.6) Exposure to vomiting – 2.4(1.0-5.5) Exposure to diarrhea – 0.8(0.5-1.3) Increased frequency of vomiting – P<0.01 Size of household – P=0.14 Onset of illness at child center (vs. onset of illness at home) – 0.9(0.6-1.6)	Primary case: a person in the child center who became ill and who had diarrhea, vomiting or nausea during the first 3 days of the outbreak Secondary case: a person who became ill from day 4 through day 12 of the outbreak Secondary household case: a person who became ill at >6 h but <10 days after the onset of disease in the corresponding patient who acquired the infection in the child center. NLV was confirmed using EM, used PCR for genotyping Power and sample size not reported 524/775 subjects (68%) returned the questionnaire	1024_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Median incubation period for primary cases 34 hours (range 2-61 hours) **Median serial interval** (between a case in the chid center and the linked household cases) Overall – 73 hours (range 4-198 hours) Counting only the first case in each household – 59 hours (range 4-198 hours) Truncating at 96 hours – 52 hours (4-96 hours)		
Becker KM, 2000 [100]	Retrospective controlled study 1,2,3,4,6,7	To investigate norovirus outbreak at a football game.	Football game in Florida. norovirus outbreak primarily involved members of the North Carolina football team during a game in Florida. N=108 members of the North Carolina team and support staff interviewed. 54 with illness: 43 primary cases and 11 secondary cases.	***Meal risk factor – Unadjusted RR (95% CI)*** Lunch 9/18 – RR 4.1 (1.6-10.0) Dinner 9/18 – RR 1.2 (0.7-2.2) Late dinner 9/18 – RR 1.2 (0.8-1.8) Breakfast 9/19 – RR 0.9 (0.6-1.5) Lunch 9/19 – RR 1.1 (0.7-1.7) Rate of attack among those who ate box lunch 9/18 – 62% ***Lunch 9/18 food specific risk factor – OR (95% CI)*** Sandwich – unadjusted OR 2.6 (1.2-5.5); adjusted OR 4.9 (1.3-18.9) Apple – unadjusted OR 1.6 (1.1-2.3); adjusted OR 2.4 (0.6-9.3) Candy bar – unadjusted OR 1.8 (1.0-3.2); adjusted OR 1.6 (0.5-5.0) Rate of attack among those with ate sandwich – 71%	All 4 stool samples obtained from North Carolina patients were positive for norovirus like virus on EM. All 4 samples and ½ stool samples from players on Florida team were positive for norovirus-like virus of genogroup I on RT-PCR. RT-PCR products had identical sequences. Power and sample size not reported	1101_IL
Parashar, U; 1998 [101]	Retrospective controlled study 1,3,4	To determine the etiologic agent, source of infection and mode of spread of a gastroenteritis outbreak.	Employees of a manufacturing company in Ohio. Demographic characteristics not reported. 325	**Symptomatic norovirus infection - Food specific attack rates** (at < 1 week after outbreak) *All results RR(95% CI)* Sandwiches – 14.1(2.0-97.3) Ice – 1.5(1.0-2.3) Tap water – 1.5(1.1-2.2) Chips – 1.4(0.9-2.1) Cookies – 1.4(0.9-2.1) Bottled soda – 1.3(0.9-1.9) Canned soda – 1.3(0.8-2.0) One of the food handlers who prepared the sandwiches reported gastroenteritis that had subsided 4 days earlier	A case was defined by the presence of vomiting or diarrhea (≥ 3 loose stools in 24 hrs). NLV was confirmed by EM and RT-PCR Power and sample size not reported	1288_RA
McEvoy, M; 1996 [102]	Retrospective controlled study	To describe an outbreak of norovirus gastroenteritis.	Passengers and crew of 4 cruises in the western Mediterranean. Median age of cases 55 years; 13/23 males	**Risk factors for symptomatic norovirus infection** (matched pairs analysis) *All results OR; P value* Gala dinner – 0.20; 0.22	A primary cabin case (the first case to have occurred in a cabin) was defined as a passenger on the ship from	1410_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
	1,3,4		46 (23 cases and 23 controls)	Salad – 1.00; 0.77 Fruit – 0.56; 0.42 Eggs – 0.50; 0.38 Table – 1.33; 1.00 Taps – OR not calculable; 0.24 Ice (tap water) – 0.56; 0.42 Teeth (tap water) – 1.00; 0.77 Pool – 0.71; 0.77 Chicken – 0.50; 0.39 Prawns – 0.29; 0.18 Meat – 1.14; 1.00 Cream – 0.67; 0.75 **Interventions** 1. Hygiene measures were introduced in the galley 2. When the passengers disembarked for a short period, the cabins were cleaned with a chlorine based disinfectant 3. Soft furnishings were removed for steam cleaning from all cabins whose occupants had reported illness. At the same time, the crew and staff quarters, including communal bathrooms and lavatories, were cleaned in the same way. **Response to outbreak** After control measures were implemented, fewer than 10 cases of diarrhea and/or vomiting were detected on each of the fifth and sixth cruises	27 May to 2 June with diarrhea (≥3 loose stools in a 24 hour period) and/or vomiting. Controls were matched to cases by sex and age (within 10 years) norovirus was identified by EM and RT-PCR in fecal specimens 277/1100 questionnaires were completed and returned. Power and sample size not reported.	
Sharp, TW; 1995 [64]	Retrospective controlled study 1,3,4,6,7	To identify risk factors for an outbreak onboard an aircraft carrier.	Crew members aboard an aircraft carrier. 4500 male crew members. Questionnaire results available for 2,618 shipboard personnel. Mean age 27 years (range, 17-59)	**Symptomatic norovirus infection - Attack rates (n=4500)** 13% with symptomatic infection 8% sought medical attention; almost all missed at ≥1 day work **Univariate analysis (n=2618)** *All results variable – attack rate; unadjusted OR (95% CI)* Age range (years) 17-19 – 17.6%; Reference 20-29 – 14.3%; 0.93 (0.6-1.5) 30-39 – 11.5%; 0.73 (0.4-1.2) 40-59 – 9.3%; 0.57 (0.3-1.2) Race White – 14.3%; Reference Black – 8.8%; 0.58 (0.4-0.85) Other – 17.2%; 1.24 (0.9-1.74)	Power and sample size not reported. Gastroenteritis was defined as anyone reporting either vomiting or water stools with at least one of the following: nausea, fever, headaches, chills, or myalgias. Gastroenteritis was associated with at least a fourfold increase in Norwalk virus antibody levels measured by ELISA.	1513_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Rank Junior enlisted – 13.8%; Reference Senior enlisted – 10.7%; 0.74 (0.4-1.3) Officers – 9.4%; 0.65 (0.4-1.09) Number of persons in sleeping compartment 1-10 – 7.1%; Reference 11-50 – 8.6%; 1.23 (0.7-2.3) 51-100 – 15.5%; 2.39 (1.4-4.3) >100 – 18.6%; 2.98 (1.7-5.3) **Multivariate analysis (n=2618)** *All results variable – adjusted OR (95% CI)* Age (by year) – 0.98 (0.97-0.99) Race White – Reference Black – 0.6 (0.3-0.9) Other – 1.0 (0.7-1.3) Number of persons in sleeping compartment 1-10 – Reference 11-50 – 1.1 (0.5-1.7) 51-100 – 2.2 (1.6-2.8) >100 – 2.8 (2.3-3.4) **Pre-outbreak antibody levels and subsequent acute gastroenteritis** *All results pre-outbreak antibody titer – No. developing illness/total No. (%)* <50 – 2/14 (14%) 50-200 – 9/28 (32%) 400-800 – 8/20 (40%) 1600-3200 – 11/35 (31%) ≥6400 – 2/12 (17%) All – 32/109 (29%) **Pre-outbreak antibody levels and subsequent fourfold or more titer rise** *All results pre-outbreak antibody titer – No. with fourfold or more titer rise/total No. (%)* <50 – 6/14 (43%) 50-200 – 12/28 (43%) 400-800 – 5/20 (25%) 1600-3200 – 9/35 (26%)	Norwalk virus like particles were also seen using immune EM in 2/6 stools.	

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				≥6400 – 2/12 (17%) All – 23/109 (31%) **Pre-outbreak antibody levels and subsequent fourfold or more titer rise with acute gastroenteritis** *All results pre-outbreak antibody titer – No. with fourfold or more titer rise and developing illness/total No. (%)* <50 – 2/14 (14%) 50-200 – 5/28 (18%) 400-800 – 4/20 (20%) 1600-3200 – 4/35 (11%) ≥6400 – 1/12 (8%) All – 16/109 (15%)		
Chadwick, PR; 1994 [103]	Retrospective controlled study 1,3,4,6,7	To determine risk factors for small round structured virus infection during an outbreak at an elderly care unit.	Healthcare workers at an elderly care unit. Cases – mean age 36 years (range 21-58 years). Controls – mean age 39 years (range 18-59 years). 90% questionnaire responders were female. 103 questionnaires returned.	**Clinical features** Overall attack rate – 34% *Attack rates among healthcare subspecialties* Nursing – 40% Pharmacists – 34% Doctors – 0% Staff absent from work due to illness – 75% Duration of absence – median 2 days (range 1-9 days) **Risk factors for symptomatic infection** *Univariate analysis* Nearby vomiting – 50% exposed staff vs. 20% unexposed staff; OR 3.89 (95% CI 1.4-11); p=0.007 Number of exposures to nearby vomiting – p=0.032 Contact with ill patients – 42% exposed staff vs. 13% unexposed staff; OR 4.71 (95% CI 0.94-46); p=0.07 Number of close contacts with ill patients – p=0.023 Cleaning vomit – OR 1.96 (95% CI 0.46-9.8); p=0.49 Cleaning diarrhea – OR 4.67 (96% CI 0.49-225); p=0.22 *Multivariate analysis* Nearby vomiting was the only significant risk factor **Interventions Implemented** Handwashing emphasized Restricted transfers from affected wards Ward closures	Case was a patient or staff at the hospital with vomiting or ≥2 loose stools in a 24 hour period. Power and sample size not reported. Aerosolization of vomit may have been important in infection transmission during the outbreak.	1555_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Staff cohorting Disinfection with chlorine-based products Attribute declining attack rates among subsequent wards to infection control measures		
Reid, JA; 1988 [104]	Retrospective controlled study 1,3,4	To investigate an outbreak of NLV.	Subjects affected by outbreak in a United Kingdom hotel in October of 1987. Over 164 people affected – 40 staff, over 70 resident guests, and 54 people attending functions. 32 cases and 100 controls completed questionnaire for case-control study.	**Symptomatic norovirus infection - Food specific attack rates** *All results: Consumption vs. no consumption; p value* *Function 2* *Smoked trout – 5/7 (71%) vs. 0/9 (0%); <0.005 Soup – 0/9 (0%) vs. 5/7 (63%); <0.005 *Cold meats* *Ham – 1/7 (14%) vs. 4/7 (57%); NS *Beef – 2/5 (40%) vs. 3/10 (30%); NS *Chicken – 2/4 (50%) vs. 3/12 (25%); NS *Tongue – ½ (50%) vs. 3/12 (25%); NS *Turkey – 2/4 (50%) vs. 2/9 (22%); NS *Pork – 1/1 (100%) vs. 4/14 (29%); NS Turkey and rice – 5/11 (45%) vs. 0/5 (0%); 0.11 *Salads* Coleslaw – 1/4 (25%) vs. 4/12 (33%); NS *Waldorf – 5/10 (50%) vs 0/6 (0%); 0.09 *Tomato and cucumber – 3/10 (30%) vs 1/5 (20%); NS *Mixed - 2/8 (25%) vs 2/7 (29%); NS *Rice - 4/6 (67%) vs 1/10 (10%); 0.04 *Function 3* *Mixed seafood – 22/28 (79%) vs 0 (0%) Baked poussin – 21/27 (78%) vs 1/1 (100%); NS Courgettes – 18/22 (82%) vs 4/6 (67%); NS Cauliflower – 19/25 (76%) vs 3/3; NS Black Forest gateaux – 19/25 (76%) vs. 3/3 (100%); NS Cream topping – 16/20 (80%) vs. 6/8 (75%); NS Cream (with coffee) – 9/12 (75%) vs. 13/16 (81%); NS Cocoa almonds: 13/15 (87%) vs 9/13 (69%); NS Table water: 6/8 (75%) vs 16/20 (80%); NS	*Foods prepared by chef who was still excreting virus 48 hours after his symptoms. Cases were guest at the hotel from October 17-24 who had gastrointestinal disease defined by the presence of vomiting, or diarrhea (3 or more loose stools in 24 hours) or abdominal pain and nausea, or fever and either abdominal pain or nausea. reported to managementbut who had not been interviewed. Norwalk-like virus identified by EM. Power and sample size not reported.	1847_IL
Iversen, AM; 1987	Retrospective controlled	To identify the source of two outbreaks	Two outbreaks occurred in the banqueting suite of a London	**Symptomatic norovirus infection - Food specific attack rates:** *All results –consumption vs. no consumption; p value*	Case was someone with abdominal pain, nausea,	1881_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
[105]	study 1,3,4	caused by a small round structured virus.	hotel. First dinner -280 guests. Second dinner – 114 guests.	*First outbreak* Melon – 197/220 vs. 0/5; 0.000006 Beef – 196/223 vs. 4/5; NS Potatoes – 196/218 vs. 3/9; NS Horseradish sauce – 142/161 vs. 58/67; NS Blackforest gateau –184/207 vs. 16/21; NS Cream – 180/202 vs. 19/26; NS *Second outbreak* Trout – 51/92 vs. 5/9; NS Horseradish sauce – 31/35 vs. 25/39; 0.026 Vermicelli consommé – 54/66 vs. 2/8; 0.004 Duck – 55/70 vs. 2/5; NS Potatoes – 52/68 vs. 4/6; NS Ice cream soufflé – 53/67 vs. 3/7; NS	vomiting, or diarrhea in a week after dinner. Chef was likely source of outbreaks. Power and sample size not reported.	
White, KE; 1986 [106]	Retrospective controlled study 1,3,4,6,7	To conduct a foodborne outbreak investigation.	Attendees at 8 banquets at a single Minnesota hotel. 383 attendees.	**Symptomatic norovirus infection - Attack rate** 220/383 (57%) developed gastroenteritis. **Food-specific attack rate** *Univariate analysis – All results % ill among exposed vs % ill among unexposed; OR; p value* *Banquet A* Potato salad – 57% vs. 30%; 3.2; 0.05 Fried chicken – 54% vs. 27%; 3.1; 0.06 Cranberry sauce – 86% vs. 34%; 11.6; 0.01 Fruit salad – 59% vs. 32%; 3; 0.07 *Banquet B* Potato salad – 82% vs. 65%; 2.5; 0.04 Coleslaw – 84% vs. 57%; 4.0; 0.0007 *Banquet C* Tossed salad – 56% vs. 13%; 9.0; 0.007 *Multivariate analysis – All results RR; p value* *Banquet A* Potato salad – 10.6; 0.010 Fried chicken – 4.1; 0.086 Cranberry sauce – 7.5; 0.062	Case was defined as individual who developed diarrhea (≥ 3 loose stools within 24 hours) or vomiting within 3 days of consuming a meal prepared by food service of the hotel or after contact with primary case. Power and sample size not reported.	1921_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Fruit salad – 7.7; 0.026 *Banquet B* Potato salad – 2; 0.177 Coleslaw – 3.8; 0.004 *Banquet C* Tossed salad – N/A		
Kaplan JE, 1982 [107] 2,4	Retrospective controlled study	To describe Norwalk oubreaks and assess how often Norwalk virus was implicated in outbreaks of acute nonbacterial gastroenteritis.	Records of gastroenteritis outbreaks investigated for a viral cause by the CDC from 1976-1980 and where serologic tests available. 7 additional norovirus outbreaks confirmed through 1980 at the NIH but not investigated by CDC.	**Overall** 31/74 outbreaks (42%) investigated by the CDC were norovirus related 17/74 outbreaks (23%) with possible involvement of the norovirus 26/74 (35%) not due to norovirus virus **Analysis of confirmed norovirus outbreaks** ***norovirus outbreak characteristics*** norovirus outbreaks: 38 confirmed including 7 not investigated by CDC 10 in camps and recreational areas, 7 in elementary schools 4 on cruise ships, 4 in nursing homes, 4 in colleges/universities, 4 in restaurants, 3 in small families, and 2 in larger communities. 3 in countries other than US, 4 on cruise ships at sea. Outbreaks occurred all months of the year. ***Source of norovirus outbreak*** Common source of infection: 31 outbreaks. 17 possible vehicle of transmission: water in 13 outbreaks (municipal water systems in 2 outbreaks, semipublic water supplies in 7, stored water on cruise ships in 2, and recreational swimming in 2 outbreaks) and food in 4 (2 with oysters and 2 with salad). Primary person to person transmission: 7 outbreaks Secondary person to person transmission (attack rates 4% to 32%): 20/ 23 common source and 3/3 person to person outbreaks for which evidence available. Secondary attack rate highest among children<10 years of age in a single outbreak where information available. ***Duration of norovirus outbreak*** Outbreak duration: median 7 days (range, 1 day to 3 months) Of 24 common source outbreaks for which information available, 12 lasted 5-9 days. Outbreaks of longer duration included 7 in which successive weekly	Common source of infection if a vehicle of transmission was incriminated by epidemiologic analysis or if the peak onset of illness occurred during the first 2 days of the outbreak. Primary person to person transmission presumed when no vehicle of transmission identified and when the peak onset of illness occurred after the second day of the outbreak; this was shown in some outbreaks by geographic clustering of cases. Secondary person to person transmission was evidenced in both types of outbreaks by the finding of illness in family members or roommates not exposed to the primary location of the outbreak. Incubation period determined by measuring either the interval between exposure to a common source and onset of illness or the intervals between	2077_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				outbreaks occurred among newly introduced populations and 1 nationwide epidemic associated with eating raw oysters Of the 5 perton to person transmitted outbreaks where information available, 4 lasted 5-9 days. ***Number of infected persons and attack rates*** Infected persons ranged from 2 to 2000. Largest outbreaks in communities, schools, recreational areas, and on cruise ships (median, 348; range, 19-2000) Smallest outbreaks in families and nursing homes (median, 19 cases; range 2-43) *All results: Common source outbreak vs. Person to person transimssion* No. affected persons – median, 236 (range, 6-2000) vs. median 38 (range 2-559). Attack rates – median, 60% (range 23%-93%) vs. median 39% (range 31% to 42%). Attack rates did not differ significantly with age or sex in the 6 outbreaks in which information was available. ***Prevalence and duration of symptoms*** *All results (#outbreaks which noted symptom): median % patients with symptom (range)* Nausea (30): 79 (51-100) Vomiting (34): 69 (25-100) Diarrhea (34): 66 (21-100) Abdominal cramps (30): 71 (17-90) Headache (22): 50 (17-80) Fever (29): 37 (13-71) Chills (14): 32 (5-74) Myalgias (14): 26 (11-73) Sore throat (7): 18 (7-32) From 5 outbreaks, vomiting more frequent than diarrhea among children; and diarrhea more frequent than vomiting among adults. In 6 elementary school outbreaks, vomiting occurred in median 75% and diarrhea in median 46% of all children In 4 ourbreaks on cruise ships (affecting mostly adults), vomiting and diarrhea occurred in 51% and 85% cases respectively Duration of illness from 29 outbreaks ranged from 2 hours to several days. The mean (or median) time was 24- 48 hours in 19 outbreaks and	onset of illness in primary and secondary cases. Serologic testing by RIA and results of stool testing by immune EM or RIA/ An outbreak of gastroenteritis was considered to be caused by norovirus if at least 50% of the serum pairs from cases had a fourfold or greater rise in Norwalk antibody titer between acute and convalescent phases. Power and sample size not reported.	

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				12- 60 hours in 26/28 outbreaks In 6 outbreaks, a small percent of persons (15% or less) were ill longer than 3 days Off 22 outbreaks that recorded incubation period of illness, range was 4-77 hours Mean (or median) incubation period was 24- 48 hours in 20/ 22 outbreaks. **Analysis of outbreaks possibly caused by norovirus virus** 17 outbreaks occurred in all seasons of the year 11 in nursing homes, 3 in camps or recreational areas, 2 in elementary schools, and 1 in college. Of 15 outbreaks in which information is available, 6 were common source infection (including 1 waterborne) and 9 primary person to person transmission (geographic clustering of cases in 2 outbreaks) Secondary transmission (attack rates, 33% to 40%) in 2/3 common source outbreaks and 6/6 person to person outbreaks where information available Outbreaks in the possibly norovirus virus category similar to in the confirmed norovirus category in duration of illness, prevalence of symptoms, and incubation period *All results: % (No. with characteristic/total number of outbreaks) among those with Norwalk infection vs. possibly Norwalk infection vs. not Norwalk infection* Duration of illness from 12 to 60 hours: 93 (28) vs. 92 (12) vs 84 (19) Vomiting ≥ 50% cases: 89 (27/30) vs. 90 (10/17) vs. 50 (18/26) Diarrhea ≥ 50% cases: 74 (27) vs. 70 (10) vs. 94 (18) Headache ≥ 50% cases: 50 (18) vs. 25 (4) vs. 38 (13) Incubation period from 24 to 48 hours: 91 (22) vs. 80 (5) vs. 78 (9) **Analysis of norovirus negative outbreaks** 26 outbreaks occurred all months of the year 5 in nursing homes, 5 in restaurants, 4 in residential communities, 4 on cruise ships, 3 in hospitals, 2 in camps or recreational areas, and 2 in colleges. 14/21 outbreaks in which information was available were relate to a		

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				common source; 7 were waterborne an 3 were foodborne (salads) 7 outbreaks were primary to primary person to person transmission; geographic clustering was found in 2 of these. Secondary transmission (attack rates 11% to 48%) in 7/7 common source outbreaks and in 2/2 person to person outbreaks for which information was available Outbreaks not due to norovirus virus similar to those due to norovirus in duration of illness, prevalence of symptoms, and incubation period		
Blanton LH, 2006 [111] 1,2,3,4	Descriptive Study	To describe epidemiologic data from outbreaks of acute gastroenteritis occurring between July 2000 and June 2004 where samples were sent to the CDC.	226 confirmed outbreaks. 184 (81%) had CaCV detected. Genogroup II norovirus strains were the most abundant (79%), followed by genogroup I norovirus strains (19%)	**CaCV** *Settings* 65% of CaCV outbreaks in nursing homes, retirement centers, and hospitals 38% outbreaks in schools and day-care centers 58% outbreaks in vacation settings including cruise ships *Transmission* Person to person transmission (55%) vs. foodborne transmission (18%); p<0.001 **norovirus** During 2002-2003 CaCV season, Farmington Hills sequivar was responsible for 36% all confirmed norovirus outbreaks and 44% of all GII outbreaks	RT-PCR used. Power and sample size not reported.	371_IL
Mattison, K; 2007 [112]	Basic Science Study Not applicable (N/A)	To assess virus survival in foods and on sufaces. FCV was used as a surrogate for norovirus to investigate its survival.	Food (lettuce, strawberry, ham) and metal surfaces. Study was conducted in Canada. N/A	**Survival of virus** *At 30 min* Lettuce – 20% Strawberry – 1% Ham – 43% Metal disk – 11% *At 7 days* There was a signifiant reduction in viral titer after 7 days for all samples at both room temperature (RT) and 4°C (P<0.05). **Comparison of virus survival at RT and 4°C (on day 7)** Lettuce – undetectable at RT; 1% survival at 4°C; statistical differences were not reported Strawberry – undetectable at both RT and 4°C; survived for 5 days at 4°C, compared with survival of 1 day at RT; statistical differences were not reported Ham – P>0.05 Metal disk – P>0.05	Power and sample size not reported	154_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Comparison of virus survival among the different samples The survival on ham was significantly greater when compared to all other surfaces at both temperatures (P<0.05)		

GRADE TABLE Q1 WHAT PERSON, VIRUS OR ENVIRONMENTAL CHARACTERISTICS INCREASE OR DECREASE THE RISK OF NOROVIRUS INFECTION IN HEALTHCARE SETTINGS?

Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**	Large Magnitude**	Dose-response	Confounders		
Person characteristics														
Demographic characteristics														
Age	Symptomatic norovirus infection*	3 OBS [62-64]	Primary attack rate was significantly increased in adults when compared with children in 1 OBS in the community setting. Secondary attack rate was significantly increased in children aged 0-5 years compared with those aged 6-10 years. Children were a possible risk factor for household transmission when compared with adults[62] Increase in age was an independent protective factor in 1 OBS among aircraft crew members [64]Children who were affected were significantly younger in 1 OBS at a mother and child health clinic [63]	Low	0	0	0	0	0	0	0	0	Low	Low
	Asymptomatic norovirus infection	1 OBS [60]	Children were a possible risk factor for detection of CaCV and norovirus GII strain when compared with adults in 1 OBS in the community setting [60]	Low	0	0	0	-1	0	0	0	0	Very Low	
	Duration of illness*	2 OBS [57,59] 1 DES [58]	Age ≥ 65 years was an independent risk factor for increased duration of diarrhea in 2 OBS in the healthcare setting [57,59] Recovery was slowest in the oldest age group ≥ 65 years in 1 DES in the nursing home setting [58]	Low	0	0	0	0	0	0	0	0	Low	
Gender	Symptomatic norovirus infection*	1 OBS[79]	Gender was not a risk factor for symptomatic norovirus infection[79]	Low	0	0	0	0	0	0	0	0	Low	Low
	Acute kidney disease	1 OBS[57]	Gender was not a risk factor for acute kidney disease[57]	Low	0	0	0	0	0	0	0	0	Low	

Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**	Large Magnitude**	Dose-response	Confounders		
	Duration of illness	1 OBS[57]	Gender was not associated with increased duration of illness[57]	Low	0	0	0	0	0	0	0	0	Low	
	Hypokalemia	1 OBS[57]	Gender was not a risk factor for hypokalemia[57]	Low	0	0	0	0	0	0	0	0	Low	
Race	Symptomatic norovirus infection*	1 OBS [64]	Black race (compared with white) was an independent protective factor in 1 OBS among aircraft crew members [64]	Low	0	0	0	-1	0	0	0	0	Very Low	Very Low
Education	Symptomatic norovirus infection*	1 OBS [61]	Education level was not a risk factor in 1 OBS in the community setting [61]	Low	0	0	0	-1	0	0	0	0	Very Low	Very Low
Patient characteristics	Symptomatic norovirus infection*	2 OBS [66,67]	Patients who were exposed to case nurses had a greater risk than those who were not in 1 OBS in the healthcare setting. Respiratory care lack of nasogastric tube care and lack of wound care were possible risk factors [67] OBS in a long term care facility, physical dependence was a possible risk factor and use of diuretics was a possible protective factor [66]	Low	0	-1	0	0	0	0	0	0	Very Low	Very low
Staff characteristics	Symptomatic norovirus infection*	1 SR [56] 2 OBS [66,67]	Patient-indexed outbreaks affected significantly more patients than staff-indexed outbreaks in 1 SR. Staff were similarly affected by both outbreak index category groups [56] Nurses who were exposed to case patients did not have a significantly different risk of infection from those who were not in 1 OBS in the healthcare setting. Being a staff member was a possible risk factor [67]. Exposure to vomitus, gastroenteritis in household and exposure to residents with gastroenteritis were possible risk factors among employees in 1 OBS in a long term care facility [66]	Low	0	0	0	0	0	0	0	0	Low	Low
	Duration of illness	1 OBS [58]	Hospital patients had a significantly increased duration of illness compared to a combined group consisting of hospital staff, nursing home staff and nursing home residents in 1 OBS [58]	Low	0	0	0	-1	0	0	0	0	Very Low	
Clinical characteristics														

Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**	Large Magnitude**	Dose-response	Confounders		
HIV	Symptomatic norovirus infection*	1 OBS [68]	HIV infected children with chronic diarrhea were a possible risk factor compared with HIV uninfected children with chronic diarrhea in 1 OBS in the healthcare setting [68]	Low	0	0	0	-1	0	0	0	0	Very Low	Very Low
	Asymptomatic norovirus infection	2 OBS [60,65]	HIV positive children were a possible risk factor compared with HIV negative children in 1 OBS in the community setting. HIV positive adults were not a risk factor [60] Presence of HIV infection or the degree of immunocompromise was not a risk factor in 1 OBS in the healthcare setting [65]	Low	0	0	0	0	0	0	0	0	Low	
Immune co-morbidities	Acute kidney disease*	1 OBS [57]	Immunosuppresive therapy was an independent risk factor for an increase in serum creatinine in 1 OBS in the healthcare setting [57]	Low	0	0	0	-1	0	0	0	0	Very Low	Very Low
Other co-morbidities	Duration of illness*	1 OBS [57]	Presence of underlying cardiovascular disorders was an independent risk factor for increased duration of vomiting in 1 OBS in the healthcare setting. Underlying malignancy and underlying trauma were independent risk factors for an increased duration of diarrhea. Presence of underlying gastrointestinal disorders was a possible risk factor for increased duration of diarrhea [57]	Low	0	0	0	-1	0	0	0	0	Very Low	Very Low
	Acute kidney disease	1 OBS [57]	Presence of underlying cardiovascular disorders and renal transplant were independent risk factors for potassium decrease in 1 OBS in the healthcare setting. Underlying trauma was a possible risk factor for an increase in serum creatinine [57]	Low	0	0	0	-1	0	0	0	0	Very Low	
Laboratory characteristics														
Antibody levels	Symptomatic norovirus/ CaCV infection*	3 OBS [74-76]	4/5 volunteers ill with norovirus showed a serum antibody rise in 1 OBS. After a second challenge, a pronounced antibody rise was again detected in these 4 subjects. The fifth ill subject maintained persistently elevated antibody levels at all times [76] Pre-existing serum CaCV antibody were a possible protective factor in 1 OBS in a Japanese orphanage [75] Uninfected subjects had a lower preexisting antibody titer than infected	Low	0	-1	0	0	0	0	0	0	Very Low	Very Low

Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**	Large Magnitude**	Dose-response	Confounders		
			subjects in 1 OBS. As the antibody titer increased, the incidence of vomiting, nausea, headache/body aches increased [74]											
Secretor genotype	Symptomatic norovirus infection*	2 OBS [70,71]	FUT2 non-secretor genotype was significantly associated with resistance to nosocomial and sporadic outbreaks of norovirus in 1 OBS [71] Presence of secretor positive genotype was associated with an increased risk in 1 OBS among volunteers challenged with norovirus [70]	Low	0	0	0	0	0	+2	0	0	High	High
	Asymptomatic norovirus infection	2 OBS [70,72]	Presence of secretor positive genotype was associated with an increased risk in 1 OBS among volunteers challenged with norovirus [70] Presence of secretor positive genotype was a possible risk factor in 1 OBS among volunteers challenged with norovirus [72]	Low	0	0	0	0	0	+2	0	0	High	
ABO phenotype	Symptomatic norovirus infection*	5 OBS [69,72,73,77,78]	Blood group O was not a risk factor in 1 OBS among volunteers challenged with norovirus [72] None of the blood types were risk factors in 2 OBS [69,77], one of which involved nosocomial and sporadic outbreaks [77] and the other involved military units [69] Blood group O was a possible protective factor in 1 OBS in the healthcare setting, although selection bias may be present [78] Blood group B was a possible protective factor in 1 OBS among volunteers challenged with norovirus [73]	Low	0	-1	0	0	0	0	0	0	Very Low	Very Low

Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**	Large Magnitude**	Dose-response	Confounders		
	Asymptomatic norovirus infection	2 OBS [72,73]	In 1 OBS among volunteers challenged with norovirus, blood group O was a possible risk factor both overall and among secretor positive patients. Blood group A was a possible protective factor overall, but not after controlling for secretor status [72] Presence of a B HBGA (B and AB blood groups combined) was a possible protective factor, as was blood group AB in 1 OBS among volunteers challenged with norovirus. Blood group O was a possible risk factor [73]	Low	0	-1	0	0	0	0	0	0	Very Low	
Virus characteristics														
Virus characteristics	Duration of illness*	1 OBS [57]	Community acquired norovirus was an independent risk factor for increased duration of vomiting in 1 OBS in the healthcare setting [57]	Low	0	0	0	-1	0	0	0	0	Very Low	Very Low
	Acute kidney disease	1 OBS [57]	Community acquired norovirus was a possible risk factor for an increase in creatinine [57]	Low	0	0	0	-1	0	0	0	0	Very Low	
	Undefined norovirus infections*	3 DES [108-110]	An increase in norovirus activity coincided with the emergence of a new GII-4 variantin 1 DES [109] GII-3a strain was identified in 100% symptomatic patients while GII-4 was identified in 27% asymptomatic patients and staff in 1 DES [110] G-II.4 strain was the predominant strain associated with outbreaks of norovirus in Australia in 1 DES [108]	Very Low	0	0	0	0	0	0	0	0	Very Low	
Environmental characteristics														
Institution characteristics	Symptomatic norovirus infection*	2 OBS [82,99]	An increase in average length of stay was an independent protective factor, general medicine ward and geriatric ward were independent risk factors in 1 OBS in the healthcare setting. Number of beds in a unit, having a previous outbreak, month following outbreak and acute care unit were possible risk factors. Surgical and mental health wards were not risk factors [82] Nurse understaffing was a possible risk factor in 1 OBS in a pediatrics	Low	0	0	0	-1	0	0	0	0	Very Low	Very Low

Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**	Large Magnitude**	Dose-response	Confounders		
			ward [99]											
Pets	Symptomatic norovirus infection*	1 OBS [61]	Pets in household and cats as pets were not risk factors in 1 OBS in the community setting [61]	Low	0	0	0	-1	0	0	0	0	Very Low	Very Low

Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**	Large Magnitude**	Dose-response	Confounders		
Diet †	Symptomatic norovirus infection*	23 OBS[61,77,80,81,84,86,89-95,97,100-102,104-107,207] and 1 DES[111]	Of 17 norovirus outbreaks in 1 OBS where a possible vehicle of transmission was identified, water was implicated in 13 (municipal water systems in 2, semipublic water supplies in 7, stored water on cruise ships in 2, and recreational swimming in 2); and food in 4 (2 with oysters and 2 with salad) [107] Person to person transmission (55%) occurred more often than food transmission (18%) in 1 DES[111] Coffee and raisin roll were independent protective factors and the number of rolls eaten was an independent risk factor in 1 OBS in the community setting where a baker continued to work despite being infected [92] Poor food-handling hygiene was independent risk factor in 1 OBS in the community setting [61] Lettuce, jalapeno peppers and onions were possible risk factors in 1 OBS in the community setting. A food handler who returned to work within a few hours of illness was identified as the source [207] Sandwiches, ice and tap water were possible risk factors in 1 OBS in the community setting. A food handler was implicated [101] Salad on Wednesday and Thursday, semolina dumpling soup on Thursday were independent risk factors and potatoes on Thursday were independent protective factors in 1 OBS in the community setting [95] Antipasti platter and garlic mashed potatoes were possible risk factors in 1 OBS in the community setting [93] Any salad, pasta salad, potato salad, vegetable salad, condiments, dips, cheese and bread were possible risk factors in 1 OBS in the community setting [86] Vegetable salad was a possible risk factor in 1 OBS in the community setting. A food handler was the source of the outbreak [97]	Low	0	0	0	0	0	0	0	0	Low	Low

Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**	Large Magnitude**	Dose-response	Confounders		
	Survival of CaCV	1 BAS [112]	Ham was a possible risk factor in 1 BAS [112]	Very Low	0	0	0	0	0	0	0	0	Very Low	
Proximity to infected persons	Symptomatic norovirus infection*	8 OBS [61,62,64,79,83,88,98,103] and 1 DES[111]	Exposure to more than one household member with gastroenteritis was an independent risk factor overall, but not when divided into two groups of age < or ≥5 years in 1 OBS in the community setting. Contact with person outside household with gastroenteritis was an independent risk factor overall and in the two age-groups [61] > 50 persons in a sleeping compartment was an independent risk factor in 1 OBS among aircraft crew members. ≤ 50 persons was not a risk factor [64] Exposure to vomiting and increased frequency of vomiting were possible risk factors in 1 OBS in the community setting. Exposure to diarrhea and the size of the household were not risk factors [62] Exposure to vomiting and increased frequency of vomiting were independent risk factors in 1 OBS in the community setting [98] Distance from the vomiter was a possible risk factor in 2 OBS in the community setting [83,88] Nearby vomiting was an independent risk factor in 1 OBS among healthcare workers. Number of exposures to nearby vomiting and number of close contacts with ill patients were possible risk factors [103] Having an ill contact was a possible risk factor in 1 OBS [79] Person to person transmission (55%) occurred more often than food transmission (18%) in 1 DES [111]	Low	0	0	0	0	0	+1	+1	0	High	High
	Time to illness	1 OBS [98]	Significantly decreased with exposure to increased frequency of vomiting in 1 OBS in the community setting [98]	Low	0	0	0	-1	0	0	0	0	Very Low	

RCT – randomized controlled trial; OBS – observational study (prospective or retrospective controlled); DES – descriptive study (case series, case report, uncontrolled data in an observational study); BAS – basic science study
* These outcomes are considered the most critical by the guideline developers.
** These modifiers can impact the GRADE by 1 or 2 points
† Rules for "not a risk factor" were not applied

Note: Definitions: "Independent risk factor" implies a variable was significant in a multivariate analysis; "possible risk factor" implies (1) it was significant in a univariate analysis and a multivariate analysis was not performed, or (2) it was significant in a univariate analysis but not in the multivariate analysis, but there were <10 events per variable examined in the multivariate analysis; "not a risk factor" implies that (1) it was not significant in a univariate/multivariate analysis when only one analysis was reported, and (2) there were > 10 events per variable examined in the univariate or multivariate analysis.

Q2: What are the best methods to identify a norovirus outbreak in a healthcare setting?

EVIDENCE TABLE Q2

Clinical criteria

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
Turcios, R; 2006 [116]	Diagnostic study 1,2	To examine how well the Kaplan's criteria, fever-to-vomiting ratio, diarrhea-to-vomiting ratio, and each component of the Kaplan criteria discriminated between outbreaks due to norovirus and due to bacterial agents. Kaplan's criteria are: 1. Vomiting in more than half of affected persons 2. Mean (or median) incubation period of 24-48 hrs 3. Mean (or median) duration of illness of 12-60 hrs 4. No bacterial pathogen in stool culture Another objective was to estimate the proportion of all outbreaks reported to the CDC between 1998 and 2000 that could be attributed to norovirus by using the Kaplan criteria alone. The gold standard for comparison was a confirmed norovirus or bacterial etiology by clinical microbiological testing and molecular biological testing.	Outbreaks reported to the CDC between 1998 and 2000. For testing the criteria, only outbreaks of confirmed etiology for which complete data were available were used. Out of a total of 4050 outbreaks, confirmed etiology with complete data were available for 362.	*All results % (95% CI) for each criterion* **Sensitivity** Kaplan criteria – 68.2(60.0-75.5) % of patients with vomiting – 88.5(82.0-93.0) Duration of illness – 85.8(78.9-90.8) Incubation period – 89.2(82.8-93.5) Fever-to-vomiting ratio – 90.1(83.6-94.3) Diarrhea-to-vomiting ratio – 96.6(91.9-98.7) **Specificity** Kaplan criteria – 98.6(95.6-99.6) % of patients with vomiting – 60.7(53.8-67.3) Duration of illness – 65.0(58.1-71.3) Incubation period – 69.6(62.9-75.6) Fever-to-vomiting ratio – 46.6(39.3-53.9) Diarrhea-to-vomiting ratio – 44.5(37.7-51.5) **Likelihood ratio** Kaplan criteria – 48.7 % of patients with vomiting – 2.2 Duration of illness – 2.4 Incubation period – 2.9 Fever-to-vomiting ratio – 1.7 Diarrhea-to-vomiting ratio – 1.7 **PPV** Kaplan criteria – 97.1(91.2-99.3) % of patients with vomiting – 60.9(54.0-67.4) Duration of illness – 62.9(55.8-69.5) Incubation period – 67.0(59.9-73.4) Fever-to-vomiting ratio – 55.7(49.0-62.2) Diarrhea-to-vomiting ratio – 55.3(48.9-61.3)	Power and sample size not reported.	348_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				NPV Kaplan criteria – 81.8(76.4-86.2) % of patients with vomiting – 88.4(81.9-92.9) Duration of illness – 86.9(80.4-91.5) Incubation period – 90.3(84.5-94.2) Fever-to-vomiting ratio – 86.3(77.7-92.0) Diarrhea-to-vomiting ratio – 94.9(87.9-98.1) **Outbreaks attributable to norovirus using Kaplan criteria** 28%		

Specimen collection

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
Duizer, E; 2007 [117]	Diagnostic study 2,3	To use statistical analysis in determining 1) the minimum number of positive stool samples using RT-PCR or ELISA (IDEIA) compared to a hypothetical gold standard needed to declare norovirus as the causative agent of a gastroenteritis outbreak and 2) the probability of finding this minimum number of positive samples for varying numbers of tested samples.	N/A	**# Positive samples needed to assign norovirus as the causative agent** ELISA: 1 positive for 2-6 samples tested RT-PCR: 1 positive for 2-4 samples tested 2 positive for 5-11 samples tested **Sensitivity (%) for detecting a norovirus outbreak for various numbers of tested samples** ELISA: 57% for 2 tested samples 72% for 3 tested samples 88% for 5 tested samples 92% for 6 tested samples RT-PCR: 84% for 2 tested samples >90% for 3 tested samples 92% for 5 tested samples 96% sensitivity for 6 tested samples	*Parameters* Defined outbreak as caused by norovirus if the prevalence is >8% Hypothetical gold standard: sensitivity 100%; specificity 100%. RT-PCR: sensitivity 72%; specificity 99%. IDEIA: sensitivity 41%; specificity 98%. Minimum # positive samples needed is the number of positive samples where there is >95% probability of attaining a prevalence ≥8%.	044_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
					IDEIA NLV (Dakocytomation Ltd., Ely, UK).	
Gray, JJ; 2007 [118]	Diagnostic study 2,3	To determine test characteristics for IDEIA and RIDA-SCREEN.	Stool samples from patients with symptoms of gastroenteritis collected during the 2004-2005 and 2005-2006 norovirus seasons and evaluated in this European multicenter study. 2,254 samples from 273 outbreaks. 274 samples collected in sporadic cases. 144 samples had other enteric pathogens identified.	**Test characteristics** IDEIA: Sensitivity 58.93% (95% CI 56.12-61.68%) Specificity 93.91% (95% CI 92.23-95.25%) PPV 92.30% NPV 64.90% RIDA-SCREEN: Sensitivity 43.81% (95% CI 41.01-46.65%) Specificity 96.27% (95% CI 95.00-97.38%) PPV 93.70% NPV 58.20% **Sensitivity for differing number of samples tested** The sensitivity for outbreak diagnosis improved when ≥6 samples tested. IDEIA: 3 vs. 6 samples tested (z=±3.191; p=0.0014) RIDA-SCREEN: 3 vs. 6 samples tested (z=±3.828; p=0.0001) **Range of norovirus genotypes detected** *All samples: Genotype - IDEIA vs. RIDASCREEN No [(%) samples genotype detected (95% CI)]; p value* GI-1 – 4 [80.00% (37.55-96.36%)] vs. 3 [60.00% (23.07-88.24%)]; 0.49 GI-2 – 11 [84.62% (57.77-95.67%)] vs. 2 [15.38% (4.33-42.23%)]; 0.0002 GI-3 – 12 [42.86% (26.51-60.93%)] vs. 9 [32.14% (17.93-50.66%)]; 0.4 GI-4 – 2 [100.00% (34.24-100.00%)] vs. 0 [0.00% (0.00-65.76%)]; 0.3 GI-5 – 3 [37.50% (13.68-69.43%)] vs. 0 [0.00% (0.00-32.44%)]; 0.2 GI-6 – 5 [71.43% (35.89-91.78%)] vs. 0 [0.00% (0.00-35.43%)]; 0.02 GI-7 – 0 [0.00% (0.00-79.35%)] vs. 0 [0.00% (0.00-79.35%)]; >0.5 GII-1 – 7 [87.50% (52.91-97.76%)] vs. 0 [0.00% (0.00-32.44%)]; 0.0024 GII-2 – 8 [50.00% (28.00-72.00%)] vs. 4 [25.00% (10.18-49.50%)]; 0.2 GII-3 – 30 [57.69% (44.19-70.13%)] vs. 11 [21.15% (12.24-34.03%)]; 0.0003 GII-4 – 203 [67.44% (61.96-72.49%)] vs. 186 [61.79% (56.19-67.10%)]; 0.17 GII-5 – 2 [33.33% (9.68-70.00%)] vs. 3 [16.67% (3.01-56.35%)]; >0.5 GII-6 – 2 [22.22% (6.32-54.74%)] vs. 0 [0.00% (0.00-29.91%)]; 0.4	IDEIA norovirus (Oxoid; Thermo Fisher Scientific, Ely, UK). RIDASCREEN norovirus (R-Biopharm, Darmstadt, Germany) RT-PCR was the reference standard.	053_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				GII-7 – 20 [68.97% (50.77-82.72%)] vs. 5 [17.24% (7.6-34.55%)]; 0.002 GII-8 – 0 [0.00% (0.00-79.35%)] vs. 0 [0.00% (0.00-79.35%)]; >0.5 GIV-1 – 0 [0.00% (0.00-48.99%)] vs. 0 [0.00% (0.00-48.99%)]; >0.5 rGII – 10 [52.63% (31.71-72.67%)] vs. 2 [10.53% (2.94-31.39%)]; 0.01 IDEIA showed reactivity to a broader range of genotypes than the RIDASCREEN norovirus assay, which showed genotype-dependent sensitivities.		
Richards, A; 2003 [119]	Diagnostic Study 1,2	To determine the test characteristics of ELISA and EM in detecting norwalk-like virus (NLV) infection when compared with PCR	Fecal samples collected from patients involved in outbreaks of gastroenteritis in the UK 531 fecal samples	**Test characteristics (%) of ELISA vs. PCR** Sensitivity – 55.5(51.1-60.0) Specificity – 98.3(97.1-99.9) PPV – 95.0(CI not reported) NPV – 76.9 (CI not reported) **Test characteristics (%) of EM vs. PCR** Sensitivity – 23.9(19.5-28.1) Specificity – 99.2(98.3-100) PPV – 93.9(CI not reported) NPV – 70.7(CI not reported) **Identification of NLV as the cause of an outbreak** (% of outbreaks) *When the causative agent was defined by ≥ 2 positive samples* EM – 7.2 ELISA – 18.6 PCR – 41.5 *When the causative agent was defined by ≥ 1 positive samples* EM – 19.6 ELISA – 47.8 PCR – 62.8 **Sensitivity; Specificity of ELISA based on number of samples collected** 2 samples – 52.9; 100 ≥4 – 69.2; 100 ≥6 – 71.4; 100 **Other results** Agreement between ELISA and PCR – 81.8% (Kappa = 0.57) Sensitivity of ELISA was significantly increased when compared with EM (P<0.01)	Power and sample size not reported.	848_RA

Diagnostic methods – Fecal specimens

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
EIA/ELISA						
Khamrin, P; 2008 [120]	Diagnostic Study 1,2	To evaluate the test characteristics of immunochromatography and ELISA (Denka) when compared with monoplex RT-PCR for detection of norovirus from stool specimens.	Infants and children with acute gastroenteritis in Japan 503 fecal specimens	**Test characteristics of immunochromatography and ELISA** *Immunochromatography vs. RT-PCR* TP – 90 TN – 375 False positive (FP) – 14 False negative (FN) – 24 Sensitivity – 78.9% Specificity – 96.4% PPV – 86.5% NPV – 94.0% Accuracy – 92.4% *ELISA vs. RT-PCR* TP – 103 TN – 375 FP – 14 FN – 11 Sensitivity – 90.4% Specificity – 96.4% PPV – 88.0% NPV – 97.2% Accuracy – 95.0% **Accuracy of norovirus genotype detection** *All results listed as positives detected/true positives* *Immunochromatography vs. RT-PCR* GI/1 – 1/2 GII/3 – 13/14 GII/4 – 75/95 GII/6 – 1/3 *ELISA vs. RT-PCR* GI/1 – 2/2	Immunochromatography takes 20 min. ELISA takes 4 hrs. Power and sample size not reported Prevalence not reported	2351_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				GII/3 – 12/14 GII/4 – 86/95 GII/6 – 3/3		
Wiechers, C; 2008 [121]	Descriptive study 1,2,3	To describe a cluster of positive IDEIA cases which were unable to be confirmed using RT-PCR or EM.	Infants in a level III neonatal intensive care unit in Germany during November 2003. 43 infants screened. 163 stool samples obtained.	**# positive/# tested samples** IDEIA: 46/163 samples from 22/43 infants were positive. RT-PCR: 0/11 samples with enough volume were positive. EM: 0/11 samples were positive. **Variables associated with IDEIA positive samples** Stools with and without blood: 11/46 vs. 1/117; p<0.001 Age of patients with IDEIA positive vs. negative samples: median 34.9 weeks (range 28.6-40.9) vs. 36.6 weeks (range 29.4-66.9); p<0.001.	RT-PCR (QIAGEN, Hilden, Germany). IDEIA NLV kit (DakoCytomation Ltd., Ely, UK).	5118_IL
Castriciano S, 2007 [122]	Diagnostic Study 1,2,3	To compare RIDASCREEN norovirus EIA to IDEIA NLV GI/GII	66 positive and 162 negative stool samples 228 total samples	**Test characteristics: Test – Positive (% sensitivity; CI) vs. Negative (% specificity; CI)** RT-PCR: 65 (98.5; 91.9-99.7) vs. 162 (100; 97.7-100) RIDASCREEN: 53 (80.3; 69.2-88.1) vs. 162 (100; 97.7-100) IDEIA-NLV: 40 (60.6; 48.5-71.5) vs. 162 (100; 97.7-100) EM: 24 (36.4; 25.8-48.4) vs. 157 (96.9; 93.0-98.7)	Used stools that had previously been screened by EM and stored at -70 C. Re-tested using RT-PCR.	143_IL
Gray, JJ; 2007 [118]	Diagnostic study 2,3	To determine test characteristics for IDEIA and RIDA-SCREEN.	Stool samples from patients with symptoms of gastroenteritis collected during the 2004-2005 and 2005-2006 norovirus seasons and evaluated in this European multicenter study. 2,254 samples from 273 outbreaks. 274 samples collected in sporadic cases. 144 samples had	**Test characteristics** IDEIA: Sensitivity 58.93% (95% CI 56.12-61.68%) Specificity 93.91% (95% CI 92.23-95.25%) PPV 92.30% NPV 64.90% RIDA-SCREEN: Sensitivity 43.81% (95% CI 41.01-46.65%) Specificity 96.27% (95% CI 95.00-97.38%) PPV 93.70% NPV 58.20% **Sensitivity for differing number of samples tested** The sensitivity for outbreak diagnosis improved when ≥6 samples tested. IDEIA: 3 vs. 6 samples tested (z=±3.191; p=0.0014) RIDA-SCREEN: 3 vs. 6 samples tested (z=±3.828; p=0.0001) **Range of norovirus genotypes detected** *All samples: Genotype - IDEIA vs. RIDASCREEN No [(%) samples genotype*	IDEIA norovirus (Oxoid; Thermo Fisher Scientific, Ely, UK). RIDASCREEN norovirus (R-Biopharm, Darmstadt, Germany) RT-PCR was the reference standard.	053_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			other enteric pathogens identified.	*detected (95% CI)]; p value* GI-1 – 4 [80.00% (37.55-96.36%)] vs. 3 [60.00% (23.07-88.24%)]; 0.49 GI-2 – 11 [84.62% (57.77-95.67%)] vs. 2 [15.38% (4.33-42.23%)]; 0.0002 GI-3 – 12 [42.86% (26.51-60.93%)] vs. 9 [32.14% (17.93-50.66%)]; 0.4 GI-4 – 2 [100.00% (34.24-100.00%)] vs. 0 [0.00% (0.00-65.76%)]; 0.3 GI-5 – 3 [37.50% (13.68-69.43%)] vs. 0 [0.00% (0.00-32.44%)]; 0.2 GI-6 – 5 [71.43% (35.89-91.78%)] vs. 0 [0.00% (0.00-35.43%)]; 0.02 GI-7 – 0 [0.00% (0.00-79.35%)] vs. 0 [0.00% (0.00-79.35%)]; >0.5 GII-1 – 7 [87.50% (52.91-97.76%)] vs. 0 [0.00% (0.00-32.44%)]; 0.0024 GII-2 – 8 [50.00% (28.00-72.00%)] vs. 4 [25.00% (10.18-49.50%)]; 0.2 GII-3 – 30 [57.69% (44.19-70.13%)] vs. 11 [21.15% (12.24-34.03%)]; 0.0003 GII-4 – 203 [67.44% (61.96-72.49%)] vs. 186 [61.79% (56.19-67.10%)]; 0.17 GII-5 – 2 [33.33% (9.68-70.00%)] vs. 3 [16.67% (3.01-56.35%)]; >0.5 GII-6 – 2 [22.22% (6.32-54.74%)] vs. 0 [0.00% (0.00-29.91%)]; 0.4 GII-7 – 20 [68.97% (50.77-82.72%)] vs. 5 [17.24% (7.6-34.55%)]; 0.002 GII-8 – 0 [0.00% (0.00-79.35%)] vs. 0 [0.00% (0.00-79.35%)]; >0.5 GIV-1 – 0 [0.00% (0.00-48.99%)] vs. 0 [0.00% (0.00-48.99%)]; >0.5 rGII – 10 [52.63% (31.71-72.67%)] vs. 2 [10.53% (2.94-31.39%)]; 0.01 IDEIA showed reactivity to a broader range of genotypes than the RIDASCREEN norovirus assay, which showed genotype-dependent sensitivities.		
Wilhelmi de Cal, I; 2007 [123]	Diagnostic study 2,3	To evaluate IDEIA and Ridascreen compared to RT-PCR for norovirus antigen detection.	The study included stool samples from children <5 years of age with acute gastroenteritis who were admitted to a hospital in Spain between October 1, 2002 and April 1, 2004. Stools collected 24-48 hrs after admission with a diagnosis of acute gastroenteritis 117 samples that were negative for bacterial	**Samples positive for norovirus** 39 samples positive by RT-PCR. Concordant results with 3 methods in 77 (65.8%) samples. Discordant results with 3 methods in 40 (34.2%) samples. 18/39 samples underwent genotyping and sequence analysis: 1 had Sapovirus and 17 were norovirus genogroup II. **Test characteristics** IDEIA: Sensitivity 76.9% Specificity 85.9% PPV 73.2% NPV 88.2% Agreement 82.9% Kappa index 0.6203 Ridascreen: Sensitivity 59% Specificity 73.1% PPV 52.3%	IDEIA NVL assay (DakoCytomation, Ely, UK). Ridascreen NLV (R-BioPharm, Darmstadt, Germany). RT-PCR assay (One-Step RT-PCR Kit, QIAGEN, Valencia, CA, USA).	144_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			pathogens, rotaviruses, adenoviruses, and astroviruses were tested for Caliciviridae by RT-PCR, IDEIA, and Ridascreen.	NPV 78.1% Agreement 68.4% Kappa index 0.3103		
De Bruin, E; 2006 [124]	Diagnostic study 2,3	To evaluate IDEIA and Ridascreen EIAs compared to RT-PCR for the diagnosis of acute gastroenteritis outbreaks.	Two panels of stool samples collected from Dutch gastroenteritis surveillance (1999 - 2003). Panel 1: 158 fecal samples from 23 outbreaks, including confirmed Rotavirus and Astrovirus outbreaks that had been tested for norovirus by RT-PCR in 2002 and 2003. Panel 2: 19 samples positive for norovirus by RT-PCR: 6 samples of 5 different genogroup I strains, 12 samples of 6 genogroup II strains, and 1 genogroup IV strain. These stool samples were	**Agreement between ELISAs and RT-PCR** Positive in all tests – 10/158 (6%) Negative in all tests – 71/158 (45%) Discrepant results – 77/158 (49%) **Detection of norovirus Samples with ELISA kits** *1. ELISA (Dako kit) vs. RT-PCR (All samples)* TP – 28 TN - 81 FN – 46 FP – 3 Sensitivity – 37.8% Specificity – 96.4% PPV – 90.3% NPV – 63.8% *2. ELISA (Dako kit) vs. RT-PCR (norovirus positive outbreaks)* <u>Criterion A – Two or more norovirus positive samples per outbreak to identify the causative agent</u> TP – 30 TN – 40 FP – 1 FN – 43 <u>Criterion B – 50% or more norovirus positive samples per outbreak to identify the causative agent</u> TP – 24 TN – 63 FP – 7 FN – 38 *3. ELISA (Ridascreen kit) vs. RT-PCR* TP – 27	RT-PCR protocol followed by Southern blot hybridization was the reference standard. IDEIA (DakoCytomation Ltd., Ely, UK). Ridascreen (R-biopharm AG, Darmstadt, Germany). Prevalence not reported	238_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			collected from Dutch gastroenteritis surveillance from 1999 to 2002.	TN - 74 FN – 47 FP – 10 Sensitivity – 36.5% Specificity – 88.1% PPV – 73.0% NPV – 61.2% *4. ELISA (Ridascreen kit) vs. RT-PCR (norovirus positive outbreaks)* Criterion A – Two or more norovirus positive samples per outbreak to identify the causative agent TP – 35 TN – 39 FP – 2 FN – 38 Criterion B – 50% or more norovirus positive samples per outbreak to identify the causative agent TP – 29 TN – 62 FP – 8 FN – 33 **Detection of norovirus outbreaks with ELISA kits** *1. ELISA (Dako kit) vs. RT-PCR* Criterion A – Two or more norovirus positive samples per outbreak to identify the causative agent TP – 8 TN – 8 FP – 0 FN – 7 Criterion B – 50% or more norovirus positive samples per outbreak to identify the causative agent TP – 5 TN – 11 FP – 0 FN – 7 *2. ELISA (Ridascreen kit) vs. RT-PCR* Criterion A – Two or more norovirus positive samples per outbreak to identify the		

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				causative agent TP – 9 TN – 8 FP – 0 FN – 6 Criterion B – 50% or more norovirus positive samples per outbreak to identify the causative agent TP – 4 TN – 11 FP – 0 FN – 8 RIDASCREEN not able to discriminate between groups 17% of PCR-identified Genogroup I 58% of PCR-identified Genogroup II 0% of PCR-identified by Genogroup IV 74/158 samples confirmed NLV via PCR and Southern Blot Of these, 28/74 confirmed with Dako and 27/74 with RIDAscreen 84/158 samples were negative by PCR 3/84 negative by PCR were positive using Dako 10/84 negative by PCR were positive using RIDAscreen Dako: 96% specificity Ridascreen: 88% specificity		
Okitsu-Negishi, S; 2006 [125]	Diagnostic study 2,3	To evaluate the RIDASCREEN norovirus ELISA kit compared to RT-PCR.	503 stool samples collected from infants and children with acute sporadic gastroenteritis who visited 6 pediatric clinics in Japan from July 2004 to March 2005.	**Test characteristics for RIDASCREEN** Sensitivity - 76.3% Specificity - 94.9%. PPV - 81.3% NPV – 93.2% 90.7% agreement FP - 20 TP -87 FN - 27 TN - 369 Sensitivity by norovirus genotype *All results – # positive/# tested (%)*	RT-PCR was the reference standard. RIDASCREEN (R-Biopharm AG, Darmstadt, Germany). Power and sample size not reported. Prevalence not reported	228_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				GI/1 – 1/2 (50%) GII/3 – 3/13 (23.1%) GII/4 – 82/96 (85.4%) GII/6 – 1/3 (33.3%)		
Burton-MacLeod, JA: 2004 [126]	Diagnostic study 2,3	To assess two enzyme-linked immunosorbent assay kits, SRSV (II)-AD and IDEIA, compared to RT-PCR.	104 stool samples with norovirus: 4 genogroup I subgroups and 10 genogroups II subgroups from 35 outbreaks that occurred in the US June 1999-2002. 33 samples with other enteric viruses from children <5 years of age with diarrhea. SRSV (II)-AD also tested with 6 Sapovirus positive samples from patients in an outbreak.	**Test characteristics** SRSV (II)-AD: Sensitivity 80% Specificity 69% 77% agreement Sensitivities > 70% for 10/14 subgroups Cross-reacted with samples containing norovirus GI and GII subgroups; as well as samples with human Sapovirus. Detected 59% of the GII antigens in the GI wells and 63% of the GI antigens in the GII wells. IDEIA: Sensitivity 39% Specificity 100% 54% agreement Sensitivities >70% for 3/14 subgroups. GII/2, GII/5, GII/6, and GII/n may not be detected by IDEIA. Discriminated between norovirus GI and GII antigens. Detected no GII antigens in the GI wells and only 7% of GI antigens in the GII wells.	SRSV (II)-AD (Denka Seiken Co. Ltd., Tokyo, Japan). IDEIA NLV (DakoCytomation Ltd., Ely, UK). RT-PCR was the reference standard. Power and sample size not reported.	660_IL
Christen, A; 2003 [127]	Diagnostic study 2,3,4	To evaluate IDEIA compared to RT-PCR in detecting norovirus.	39 stool samples from a prior case-control study conducted in Switzerland. 24 additional samples previously PCR tested by a German Laboratory.	**Swiss samples** TP – 9 TN – 15 FN - 12 FP - 3 *IDEIA Test characteristics* Sensitivity 0.43 Specificity 0.83 PPV 0.75 NPV 0.56 Relative trueness 0.62	IDEIA NLV ELISA (Dako-Cytomation, Ely, UK). RT-PCR was the reference standard. Power and sample size not reported. Prevalence not reported Differences in sensitivities may have resulted from differences in storage of samples (4ºC for	4519_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				False positive 0.17 False negative 0.57 Concordance index Kappa 0.25 **German samples** TP – 6 TN – 11 FN - 7 FP – 0 *IDEIA Test characteristics* Sensitivity 0.46 Specificity 1.00 PPV 1.00 NPV 0.61 Relative trueness 0.71 False positive 0.00 False negative 0.54 Concordance index Kappa 0.44	<3 days versus -20ºC for long term storage as recommended by the manufacturer). Some samples had been stored for many weeks at 4ºC.	
Gunson, R; 2003; [128]	Diagnostic study 1	To compare a real-time polymerase chain reaction (PCR) and a newly developed EIA for the detection of norovirus. Negative or discrepant PCR results were investigated using EM and a different, not real time PCR.	Stool samples were collected from outbreaks and sporadic cases/unidentified outbreaks, no timeframe specified 70 stool samples	**Positive samples detected** *1. PCR* Overall – 26 Among sporadic cases – 5 *2. EIA* Overall – 10 Among sporadic cases – 3 All PCR samples could be confirmed using the second PCR. The EIA detected two positive samples that were negative by the PCR. Neither of these samples could be confirmed using the second PCR or EM. EIA: Positive / Negative Real-time PCR – Positive: 8 / 18 Real-time PCR – Negative: 2 / 42 **Test characteristics (%)** Sensitivity – 30.8 Specificity – 95.5 PPV – 80.0	Power and sample size not reported. Prevalence not reported	757_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				NPV – 70.0		
Rabenau, H; 2003 [17]	Diagnostic Study 1,2	To compare the sensitivity and specificity of: 1. ELISA when compared with a) TEM and PCR or b) PCR only 2. TEM when compared with a) ELISA and PCR or b) PCR only	Inhabitants and employees of homes for the elderly (in Frankfurt, Germany) aged 20 to >60 years; 73% females, 42% > 60 yrs. 244 stool samples from 227 patients	**Test characteristics (%) for ELISA** *When compared with TEM and PCR* Sensitivity – 50.0 Specificity – 96.2 PPV – 68.0 NPV – 92.2 (True Positive[TP] – 17; True Negative[TN] – 202; FP – 8; FN – 17) *When compared with PCR only* Sensitivity – 31.3 Specificity – 94.9 PPV – 60.0 NPV – 84.9 (TP – 15; TN – 186; FP – 10; FN – 33) **Test characteristics (%) for TEM** *When compared with ELISA and PCR* Sensitivity – 88.2 Specificity – 99.0 PPV – 93.8 NPV – 98.1 (TP – 30; TN – 208; FP – 2; FN – 4) *When compared with PCR only* Sensitivity – 58.3 Specificity – 98.0 PPV – 87.5 NPV – 90.6 (TP – 28; TN – 192; FP – 4; FN – 20) **Test characteristics (%) for PCR** *When compared with ELISA and TEM* Sensitivity – 94.1 Specificity – 92.4 PPV – 66.7 NPV – 99.0 (TP – 32; TN – 194; FP – 16; FN – 2)	Power and sample size not reported. Prevalence not reported	801_RA
Richards, A; 2003 [119]	Diagnostic Study 1,2	To determine the test characteristics of ELISA and EM in detecting norwalk-like virus (NLV) infection when	Fecal samples collected from patients involved in outbreaks of	**Test characteristics (%) of ELISA vs. PCR** Sensitivity – 55.5(51.1-60.0) Specificity – 98.3(97.1-99.9) PPV – 95.0(CI not reported)	Power and sample size not reported. Prevalence not reported	848_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
		compared with PCR	gastroenteritis in the UK 531 fecal samples	NPV – 76.9 (CI not reported) **Test characteristics (%) of EM vs. PCR** Sensitivity – 23.9(19.5-28.1) Specificity – 99.2(98.3-100) PPV – 93.9(CI not reported) NPV – 70.7(CI not reported) **Identification of NLV as the cause of an outbreak** (% of outbreaks) *When the causative agent was defined by ≥ 2 positive samples* EM – 7.2 ELISA – 18.6 PCR – 41.5 *When the causative agent was defined by ≥ 1 positive samples* EM – 19.6 ELISA – 47.8 PCR – 62.8 **Sensitivity; Specificity of ELISA based on number of samples collected** 2 samples – 52.9; 100 ≥4 – 69.2; 100 ≥6 – 71.4; 100 **Other results** Agreement between ELISA and PCR – 81.8% (Kappa = 0.57) Sensitivity of ELISA was significantly increased when compared with EM (P<0.01)		
EM						
Rabenau, H; 2003 [17]	Diagnostic Study 1,2	To compare the sensitivity and specificity of: 1. ELISA when compared with a) TEM and PCR or b) PCR only 2. TEM when compared with a) ELISA and PCR or b) PCR only	Inhabitants and employees of homes for the elderly (in Frankfurt, Germany) aged 20 to >60 years; 73% females, 42% > 60 yrs. 244 stool samples from 227 patients	**Test characteristics (%) for ELISA** *When compared with TEM and PCR* Sensitivity – 50.0 Specificity – 96.2 PPV – 68.0 NPV – 92.2 (True Positive[TP] – 17; True Negative[TN] – 202; FP – 8; FN – 17) *When compared with PCR only* Sensitivity – 31.3 Specificity – 94.9 PPV – 60.0 NPV – 84.9	Power and sample size not reported. Prevalence not reported	801_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				(TP – 15; TN – 186; FP – 10; FN – 33) **Test characteristics (%) for TEM** *When compared with ELISA and PCR* Sensitivity – 88.2 Specificity – 99.0 PPV – 93.8 NPV – 98.1 (TP – 30; TN – 208; FP – 2; FN – 4) *When compared with PCR only* Sensitivity – 58.3 Specificity – 98.0 PPV – 87.5 NPV – 90.6 (TP – 28; TN – 192; FP – 4; FN – 20) **Test characteristics (%) for PCR** *When compared with ELISA and TEM* Sensitivity – 94.1 Specificity – 92.4 PPV – 66.7 NPV – 99.0 (TP – 32; TN – 194; FP – 16; FN – 2)		
Richards, A; 2003 [119]	Diagnostic Study 1,2	To determine the test characteristics of ELISA and EM in detecting norwalk-like virus (NLV) infection when compared with PCR	Fecal samples collected from patients involved in outbreaks of gastroenteritis in the UK 531 fecal samples	**Test characteristics (%) of ELISA vs. PCR** Sensitivity – 55.5(51.1-60.0) Specificity – 98.3(97.1-99.9) PPV – 95.0(CI not reported) NPV – 76.9 (CI not reported) **Test characteristics (%) of EM vs. PCR** Sensitivity – 23.9(19.5-28.1) Specificity – 99.2(98.3-100) PPV – 93.9(CI not reported) NPV – 70.7(CI not reported) **Identification of NLV as the cause of an outbreak** (% of outbreaks) *When the causative agent was defined by ≥ 2 positive samples* EM – 7.2 ELISA – 18.6 PCR – 41.5 *When the causative agent was defined by ≥ 1 positive samples*	Power and sample size not reported Prevalence not reported	848_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				EM – 19.6 ELISA – 47.8 PCR – 62.8 **Sensitivity; Specificity of ELISA based on number of samples collected** 2 samples – 52.9; 100 ≥4 – 69.2; 100 ≥6 – 71.4; 100 **Other results** Agreement between ELISA and PCR – 81.8% (Kappa = 0.57) Sensitivity of ELISA was significantly increased when compared with EM (P<0.01)		
PCR						
Nordgren, J; 2008 [129]	Diagnostic study 2,3	To evaluate 2 novel light-upon-extension (LUX) RT-PCR assays for norovirus genogroup I and II detection and quantification.	61 stool samples from Sweden. 42 samples from Nicaragua. A reference panel of 15 stool samples from Sweden used for external validation of norovirus.	**Positive samples** *Overall* - 99% correlation between LUX RT- PCR and TaqMan RT-PCR. LUX RT-PCR – 47/103 Conventional PCR – 39/103 TaqMan RT-PCR – 48/103 *Swedish samples* LUX RT-PCR and TaqMan RT-PCR – 18/61 (100% correlation). *Nicaraguan samples* LUX RT-PCR – 29/42 TaqMan RT-PCR – 30/42 Conventional PCR – 25/42 IDEIA – 24/42 *Reference panel* LUX RT-PCR correctly identified all (n=11) coded controlled specimens. **Detection level** LUX RT- PCR detected ≤ 10^1 to 10^7 genes/reaction, with a theoretical lower limit of ≤ 20,000 viruses/gm of stool.	TaqMan based RT-PCR described by Kageyama, conventional PCR described by Zintz were used as the reference standards for both the Swedish and Nicaraguan samples. IDEIA (DakoCytomation, Copenhagen, Denmark) was used as a reference for the Nicaraguan specimens. Power and sample size not reported.	5115_IL
DeMedici, D; 2007 [130]	Diagnostic study 1,2,3	To compare IDEIA, a published RT-PCR, and an RT-boosted-PCR in detecting norovirus in stools collected after the end of a	Samples obtained from an outbreak in Italy in December 2002 where 202 patients developed	**Positive samples** ELISA – 6/41 RT-PCR – 6/41 RT-boosted-PCR – 23/41	IDEIA NLV kit (Dako, Ely, UK) Power and sample size not reported.	049_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
		gastroenteritis outbreak.	vomiting and/or diarrhea after eating oysters. 41 stool samples.	Results of RT-PCR vs. ELISA (χ^2=0.17; p>0.05). RT-boosted-PCR vs. RT-PCR and ELISA (χ^2=15.06 and 13.47; p<0.05 for both).		
Hymas, W; 2007 [131]	Diagnostic study 2,3	To evaluate a novel one step real-time eclipse RT-PCR designed to detect norovirus genogroups I and II compared to conventional CDC TaqMan assay.	29 stool samples and 9 RNA samples provided from Utah and North Carolina.	**Correlation between eclipse RT-PCR and TaqMan PCR** 97% overall agreement *By genotype:* Genotype I: 100% correlation Positive by both tests – 4 Negative by both tests – 32 Genotype II: 91% correlation Positive by both tests – 25 Negative by both tests – 10 Discordant results - 3 1 stool sample was positive by eclipse RT-PCR but negative by TaqMan PCR. 2 samples were positive by eclipse RT-PCR but indeterminate by TaqMan PCR. **Limit of detection and cross reactivity** Sensitivity for GI and GII was approximately 50 copies/reaction.	CDC Taqman assay was the reference standard. Power and sample size not reported.	130_IL
Logan, C; 2007 [132]	Diagnostic study 2,3	To test real-time RT-PCR compared to EM in detecting viral gastroenteritis, including norovirus, Sapovirus, and human Astrovirus.	Stool samples from pediatric patients with diarrhea and/or vomiting received at a microbiology laboratory in Ireland, from February 2004-April 2005. 140 stool samples from symptomatic patients. 25 stool samples from asymptomatic patients.	**Positive results** Enteric viruses were detected in 53/140 (38%) samples by RT-PCR vs. 10/140 (8%) by EM. Detection of norovirus increased 200% using RT-PCR over EM. All norovirus samples were genogroup II/4. **Agreement between EM and RT-PCR** *norovirus* Positive by both tests – 5 Negative by both tests – 109 Discordant results – 26 4 were positive by EM but negative by RT-PCR. 22 were negative by EM but positive by RT-PCR. **Test characteristics (%) of RT-PCR vs EM** Sensitivity – 55.6 Specificity – 83.2 PPV – 18.5 NPV – 96.5	EM was the reference standard. Power and sample size not reported.	008_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
Menton, JF; 2007 [133]	Diagnostic study 1,3	To evaluate a real-time RT PCR and a Reverse Line Blot Hybridization assay developed based on the open reading frame (ORF)1-ORF2 region. The assays were validated using a reference stool panel and then used to investigate two outbreaks of gastroenteritis.	Reference stool panel contained 5 genotypes of GI norovirus and 9 genotypes of GII norovirus. 56 samples from two norovirus outbreaks in Irish hospitals in 2005 and 2006.	**Level of detection** GI – 10^7 to 10^1 molecules of plasmid DNA GII – 5 x 10^7 to 5 x 10^1 molecules of plasmid DNA **Positive results** 26/56 samples positive. All belonged to the GII/4 variant.	Power and sample size not reported.	052_IL
Wolf, S; 2007 [134]	Diagnostic study 2,3	To evaluate a multiplex real-time RT-PCR that distinguishes between norovirus genogroups I, II, and III and targets the junction between open reading frames 1 and 2 compared to Kageyama real time RT-PCR.	Real time RT-PCR assays evaluated against 45 RNA stool samples collected from 2001-2006 known to be positive for norovirus including: 34 human stool samples from New Zealand, 6 raw and 3 treated sewage samples, and single samples of contaminated drinking water and source water. 28 stool samples collected from asymptomatic cattle in May 2006 from farms in New Zealand.	**Positive results** Multiplex real time RT-PCR positive for norovirus GI/1, GI/2, GI/3, GI/4, GI/5, GI/6, G1/7, GII/8, GII/10, GII/12, and GII/17 in different matrices (stool samples, treated and raw sewage, source water, and treated drinking water). **Agreement between the multiplex real time RT-PCR vs. Kageyama real time RT-PCR** All samples positive by Kageyama RT-PCR also positive by multiplex RT-PCR. Norovirus GI – 2/25 (8%) negative by Kageyama RT-PCR but positive by multiplex RT-PCR. Norovirus GII – 3/17 (18%) negative by Kageyama RT-PCR but positive by multiplex RT-PCR. **Cycle threshold (C_T) values** In 16/20 norovirus GI samples and 26/28 norovirus GII samples positive by both assays, C_T values for the multiplex assay were on average -2.4 C_T U lower than for the Kageyama assay. Remaining 6 samples had higher C_T values using the multiplex assay: 3/3 GI/3 specimens, on average +3.9 C_T U 1/1 GI/7 specimen, +3.5 C_T U 1/1 GII/1 specimen, +3.3 C_T U 1/1 GII/12, +1.4 C_T U **Level of detection** Multiplex real-time RT-PCR detects <10 copies/reaction of norovirus GI/1, GII/3, and GIII/1. Calculated efficiency values of the assay were 0.93, 0.90, and 1.04 based on the slopes of the standard curves of 3.59, 3.60, and 3.23.	Kageyama real time RT-PCR compared to the multiplex real time RT-PCR. A new bovine NLV, Bo/NLV/Norsewood/2006/NZL was identified using multiple real-time RT-PCR. Power and sample size not reported.	068_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
Yoda, T; 2007 [135]	Diagnostic study 2,3	To evaluate a one-step reverse transcription loop-mediated isothermal amplification (RT-LAMP) assay in comparison to routine RT-PCR.	94 samples from Japan obtained during 2004-2006 which had previously been analyzed for bacterial and enteric viruses .	**Agreement between RT-LAMP (OPH) vs. RT-PCR (Eiken)** *All results – RT-LAMP (OPH) vs. RT-PCR (Eiken) # positive/# samples* GI/1 – 1/1 vs. 1/1 GI/3 – 7/7 vs. 3/7 GI/4 – 3/3 vs. 3/3 GI/8 – 4/4 vs. 4/4 GI/11 – 2/2 vs. 0/2 GI/12 – 8/8 vs. 2/8 GII/2 – 10/10 vs. 10/10 GII/3 – 10/10 vs. 10/10 GII/4 – 10/10 vs. 10/10 GII/6 – 10/10 vs. 10/10 GII/12 – 2/2 vs. 2/2 GII/1 – 3/5 vs. 4/5 GII/5 – 4/4 vs. 4/4 GII/7 – 3/3 vs. 3/3 **Sensitivity tests** *All results –No. of copies in clinical sample – sensitivity RT-LAMP (OPH) vs. sensitivity RT-PCR (Eiken)* GI/3 – 8×10^5 – 8×10^1 vs. 8×10^4 GI/8 – 8×10^4 – 8×10^{-1} vs. 8×10^{-1} GII/2 – 7×10^4 – 7×10^0 vs. 7×10^1 GII/3 – 8×10^3 – 8×10^1 vs. 8×10^3 GII/4 – 5×10^6 – 5×10^1 vs. 5×10^1 GII/6 – 2×10^5 – 2×10^2 vs. 2×10^2 The results of RT-LAMP correlated well to RT-PCR.	EC NLV GI and GII detection kits (Eiken Chemical Co., Ltd.) Power and sample size not reported.	167_IL
Antonishyn, NA; 2006 [136]	Diagnostic study 2,3	To evaluate a one-step real-time multiplex RT-PCR compared to conventional PCR.	150 stool samples from cases of acute nonbacterial gastroenteritis between November 2004-March 2005. 50 archived samples used to compare TaqMan PCR with a separate RT using random primers or	**Agreement between one-step multiplex RT-PCR vs. conventional PCR** Both tests positive - 59 Both tests negative - 27 Discordant results – 14 14 were negative by conventional RT-PCR but positive using one-step real-time RT-PCR. Sensitivity of multiplex RT-PCR 19% higher than manual extraction with conventional RT-PCR.	Power and sample size not reported.	223_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			a single-step RT-PCR. 100 samples used to compare sensitivity of multiplex PCR with conventional RT-PCR.			
Trujillo, A; 2006 [18]	Diagnostic study 2	To compare the test characteristics of Taqman RT-PCR with conventional RT-PCR for the detection of GI, GII and GIV strains	Stool specimens from sporadic cases and outbreaks of gastroenteritis. Water samples from outbreaks of gastroenteritis in the US. 92 stool samples and 33 water samples	**Test characteristics of Taqman RT-PCR vs. conventional RT-PCR** *Stool specimens* TP – 65 TN – 27 FP – 0 FN – 0 By means of serially diluted norovirus RNA transcripts, a potential detection limit of < 10 transcript copies per reaction mixture was observed with the GII assay and a potential detection limit of < 10 transcript copies per reaction mixture was observed with the GI assay. *Water specimens* 8/33 specimens were found to be positive. No test characteristics were reported	Power and sample size not reported	4225_RA
Hohne, M; 2004 [137]	Diagnostic study 2,3	To evaluate a one-tube RT-PCR method, which would prevent the product carryover, in comparison to an in-house RT-PCR.	70 positive stool samples from outbreaks in Germany and 34 European samples collected over a 4 year period (1997-2000).	**Positive detection by one-tube RT-PCR of previously identified positive stool samples** Overall 93% detection including isolates of 4 different GGI and 7 different GGII genotypes. German outbreaks – 66/70 (94.3%) samples were positive including those of 6 different GGII genotypes and 2 different GGI genotypes. European samples –31/34 (91%) samples were positive including those of 4 different GGI genotypes and 7 different GGII genotypes.	Samples had previously been diagnosed positive via PCR or EM.	3090_IL
Rohayem, J; 2004 [138]	Diagnostic study 2,3	To evaluate a single-step multiplex RT-PCR compared to simplex RT-PCR for norovirus, Astrovirus, and Adenovirus.	460 stool samples from infants or children in Germany with non-Rotavirus acute gastroenteritis during 14 months	**Detection limit of the multiplex RT-PCR** Detection limit of 10^2 copies for norovirus and Astrovirus RNA transcript, and adenovirus plasmid DNA. **Positive tests** *Retrospective collection (n=257)* norovirus:	IDEIA Astrovirus and norovirus genogroup I and II, Dako, Germany. Acute gastroenteritis defined as ≥ 1 episode of diarrhea (watery or loose stools in a 24 hour	668_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			(March 1997 to May 1998): 257 archived samples 203 rotavirus-negative samples collected prospectively	Simplex RT-PCR – 17 (6.6%) Multiplex RT-PCR – 17 (6.6%)	period), with vomiting and/or other symptoms (fever, nausea, abdominal pain, and/or cramps).	
Schmid, M; 2004 [139]	Diagnostic study 2,3	To evaluate a real-time RT-PCR assay on the LightCycler (LC) with SYBR Green detection and melting curve analysis (T_m) compared to RIDASCREEN.	52 stool samples from Germany between January-April 2003: 38 from patients in gastroenteritis outbreaks 14 single sporadic cases in children <5 years of age 13.1% were < 10 years of age, 39.5% between 10-60 years, and 47.4% were > 60 years old	**Positive cases** Antigen ELISA – 18/52 (34.6%) samples positive Real-time PCR and nPCR – 26/52 (50%) samples positive **Agreement between real-time PCR, antigen ELISA, and nPCR** Positive by all three tests – 9 Negative by all three tests – 17 Positive by real-time PCR and nPCR but negative by ELISA – 17 Positive by ELISA but negative by real-time PCR and nPCR – 9 100% correlation between real-time PCR and nPCR. **Test characteristics compared to nested PCR** ELISA – sensitivity 9/26 (34.6%) and specificity 17/26 (65.3%) Real-time PCR – sensitivity 26/26 (100%) and specificity 26/26 (100%) Difference in sensitivity between ELISA and real-time PCR (34.6% vs. 100%; p<0.001) PCR-based procedures are more sensitive and specific than antigen ELISA.	RIDASCREEN Norwalk-like virus kit (R-Biopharm, Darmstadt, Germany) and well-established nested PCR used as reference standards.	655_IL
Vinje J, 2003 [140]	Diagnostic study 2,3	To evaluate the performance of 5 different RT-PCR assays for the detection of norovirus in an international collaborative study.	5 laboratories in 5 countries in the European consortium tested stool specimens collected over a 4 year period (1997 to 2000) from both outbreaks and sporadic cases of gastroenteritis and had previously	**Overall characteristics** Norovirus detected by at least 1 RT-PCR assay in 69 (84%) of the samples that originally tested positive. Overall sensitivity: 52-73% overall Overall sensitivity by genotype: 54-100% for genogroup I vs. 58-85% for genogroup II Overall sensitivity by test: p1 67% vs. p2 59% vs. p5 52% vs. p6 73% vs. p13 60% 64% of false-negative results in a set of diluted stools (n=20) that may have lost quality upon storage. Sensitivity improved when these samples were excluded. No single assay was best although the p1 assay demonstrated the most satisfactory overall performance.	PCR assays: Laboratory p1 use primer pair JV12-JV13 Laboratory p2 use NVp110 followe by PCR with the primers NVp110, Ni, an NVp69 Laboratory p5 used two RT-PCR assays with E3-Ni an E3-Ando primer pairs respectively Laboratory p6 use nested RT-PCR assay format Laboratory p13 use single tube RT-PCR targeting the 3' en of	IL_836

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			been tested by RT-PCR and EM. 91 stool samples – 82 norovirus positive and 9 controls	**Sensitivity by genotype** GI genotype: p1 100%, p2 54%, p5 85%, p6 92%, p13 85% GII genotype: p1 75%, p2 75%, p5 58%, p6 85%, p13 69%	ORF1 (region B)	
Tatsumi, M; 2002 [141]	Diagnostic study 1,2	To determine the sensitivity and specificity of RT-PCR-ELISA for detecting Norwalk virus when compared with conventional PCR	Children aged 2 months to 14 years (mean age 28.7 months) admitted with acute gastroenteritis. Study was conducted in Japan. 93 children; 154 stool samples	**Test characteristics** All 46 stool specimens that were positive for viruses other than Norwalk by RT-PCR-Southern hybridization were identified as such by RT-PCR-ELISA All 30 stool specimens that were positive for Norwalk virus by RT-PCR-Southern hybridization were identified as such by RT-PCR-ELISA In terms of detection limits, the sensitivity of RT-PCR-ELISA was the same as that of conventional PCR with Southern hybridization and was 10-100 times more sensitive than the conventional PCR. In 93 other stool specimens from hospitalized patients, 20% samples were found to be positive with RT-PCR-ELISA and 13% were found to be positive with conventional PCR.	Power and sample size not reported	911_RA
O'Neill, H; 2001 [142]	Diagnostic study 1	To assess the use of nRT-PCR in detecting norovirus	31 outbreaks in various settings including nursing homes, small district hospitals, large general hospitals, a ferry ship, hotels, restaurants and staff canteens. Study was conducted in the UK. Total N not reported	**Number of samples positive for norovirus** (follow-up not reported) *All results number positive/number tested; percentage positive* Ferry ship – 8/10; 80 (All 10 specimens negative for virus by EM) Country hotel – 14/17; 82 (2 positive by EM) Nursery school – 7/12; 50 City hotel – 3/3; 100 Restaurant – 8/32; 25 Restaurant – 7/7; 100 Large hospital – 14/116; 12 Psychiatric hospital – 27/35; 77 Restaurant – 5/5; 100 Large hospital – 16/58; 27 Medical ward – 9/17; 53 District hospital – 8/32; 25 Medical ward – 3/5; 60 Nursing home – 2/2; 100 Nursing home – 2/2; 100 Large Hospital – 7/37; 19 District hospital – 2/2; 100 Care of elderly ward – 9/12; 75	Power and sample size not reported Simultaneous testing with EM was done only for the first two outbreaks	983_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Nursing home – 2/5; 40 Hotel – 8/10; 80 Hotel – 6/12; 50 Large area hospital – 12/67; 18 Hotal – 3/3; 100 Regimental reunion – 9/11; 82 Leisure center – 4/6 - 66		
NASBA						
Jean, J; 2003 [143]	Diagnostic study 2	To evaluate the sensitivity of NASBA primers specific for the GII norovirus adapted for RT-PCR and the effect of transcriptional enhancement (TE) both followed by electrochemiluminescence (ECL).	Stool specimens from regional gastroenteritis outbreaks. Study conducted in North Carolina Not reported	**Sensitivity of NASBA derived RT-PCR** Comparable to other RT-PCR protocols. Consistent detection of viral RNA by RT-PCR was obtained up to approximately -7 log_{10} dilution with ECL readings ranging from 3.2 to 3.6 log_{10} **Sensitivity of NASBA derived RT-PCR/TE** A detection limit of ≥1 log_{10} was observed with ECL readings ranging from 4.3 to >7.0 log_{10}	Power and sample size not reported	5780_RA
Greene, S; 2003 [144]	Diagnostic study 1,2	To determine the test characteristics of a rapid NASBA when compared with RT-PCR for the detection of Norwalk-like viruses (NLV)	Volunteers challenged with norovirus. Demographics not reported. Study setting unclear. 15 stool specimens	**Detection limits** The NASBA assay could consistently detect 10^5-10^2 detectable units of NLV RNA in a stool filtrate. **Cross-reactivity** Cross-reactivity studies with a representative panel of other enteric pathogens were negative **Sensitivity** 100% **Specificity** 50% **Accuracy** 67%	Power and sample size not reported	856_RA

Diagnostic methods – Food specimens

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
PCR						
Tian, P; 2006 [145]	Diagnostic Study 2	To develop a sensitive RT – Immuno PCR method for detecting norovirus capsid protein in food samples	Food samples contaminated with norovirus. Study was conducted in the US. N/A	**Detection limit of RT-Immuno PCR compared with ELISA and conventional RT-PCR** Viral RNA could be detected in samples diluted 1000 fold when compared with ELISA and 10-100 fold when compared with RT-PCR using fecal and food samples	Power and sample size not reported	4285_RA

Diagnostic methods – Water specimens

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
PCR						
Wolf, S; 2007 [134]	Diagnostic study 2,3	To evaluate a multiplex real-time RT-PCR that distinguishes between norovirus genogroups I, II, and III and targets the junction between open reading frames 1 and 2 compared to Kageyama real time RT-PCR.	Real time RT-PCR assays evaluated against 45 RNA samples collected from 2001-2006 known to be positive for norovirus including: 34 human stool samples from New Zealand 6 raw and 3 treated sewage samples Single samples of contaminated drinking water and source water.	**Positive results** Multiplex real time RT-PCR positive for norovirus GI/1, GI/2, GI/3, GI/4, GI/5, GI/6, G1/7, GII/8, GII/10, GII/12, and GII/17 in different matrices (stool samples, treated and raw sewage, source water, and treated drinking water). **Agreement between the multiplex real time RT-PCR vs. Kageyama real time RT-PCR** All samples positive by Kageyama RT-PCR also positive by multiplex RT-PCR. norovirus GI – 2/25 (8%) negative by Kageyama RT-PCR positive by multiplex RT-PCR. norovirus GII – 3/17 (18%) negative by Kageyama RT-PCR positive by multiplex RT-PCR. **Cycle threshold (C_T) values** In 16/20 norovirus GI samples and 26/28 norovirus GII samples positive	Kageyama real time RT-PCR compared to the multiplex real time RT-PCR. A new bovine NLV, Bo/NLV/Norsewood/2006/NZL was identified using multiple real-time RT-PCR.	068_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			28 stool samples collected from asymptomatic cattle in May 2006 from farms in New Zealand.	by both assays, C_T values for the multiplex assay were on average -2.4 C_T U lower than for the Kageyama assay. Remaining 6 samples had higher C_T values using the multiplex assay: 3/3 GI/3 specimens, on average +3.9 C_T U 1/1 GI/7 specimen, +3.5 C_T U 1/1 GII/1 specimen, +3.3 C_T U 1/1 GII/12, +1.4 C_T U **Level of detection** Multiplex real-time RT-PCR detects <10 copies/reaction of norovirus GI/1, GII/3, and GIII/1 N/A. Calculated efficiency values of the assay were 0.93, 0.90, and 1.04 based on the slopes of the standard curves of 3.59, 3.60, and 3.23.		
Trujillo, A; 2006 [18]	Diagnostic study 2	To compare the test characteristics of Taqman RT-PCR with conventional RT-PCR for th edetection of GI, GII and GIV strains	Stool specimens from sporadic cases and outbreaks of gastroenteritis. Water samples from outbreaks of gastroenteritis in the US. 92 stool samples and 33 water samples	**Test characteristics of Taqman RT-PCR vs. conventional RT-PCR** *Stool specimens* TP – 65 TN – 27 FP – 0 FN – 0 By means of serially diluted norovirus RNA transcripts, a potential detection limit of < 10 transcript copies per reaction mixture was observed with the GII assay and a potential detection limit of < 10 transcript copies per reaction mixture was observed with the GI assay. *Water specimens* 8/33 specimens were found to be positive. No test characteristics were reported	Power and sample size not reported	4225_RA
Concentration method						
Beuret, C; 2003[146]	Diagnostic study None	To test a method for concentration of enteric viruses from water, whereby viruses are directly lysed after filtration on a negatively charged membrane. This method does not have the rinsing, elution, centrifugation and flocculation steps used in	Water samples. Study was conducted in Switzerland. Not reported	**Detection limit** A sensitivity of a 10^6 fold dilution could be detected for norovirus which compared favorably to the older protocol	Power and sample size not reported	5853_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
		older protocols.				

GRADE TABLE Q2 WHAT ARE THE BEST METHODS TO IDENTIFY A NOROVIRUS OUTBREAK IN A HEALTHCARE SETTING?

Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**		
Kaplan criteria	Sensitivity*	1 DIAG [116]	68%	High	0	0	0	-1	0	Moderate	Moderate
	Specificity*	1 DIAG [116]	99%	High	0	0	0	-1	0	Moderate	
	PPV*	1 DIAG [116]	97%	High	0	0	0	-1	0	Moderate	
	NPV*	1 DIAG [116]	82%	High	0	0	0	-1	0	Moderate	
Specimen collection	Number of positive samples needed*	1 DIAG [117]	Using ELISA, 1 positive sample for 2-6 samples tested was needed to assign norovirus as the causative agent Using RT-PCR, 1 positive sample for 2-4 samples tested or 2 positive samples for 5-11 samples tested were needed to assign norovirus as the causative agent	High	-1	0	0	-1	0	Low	Low
	Sensitivity*	2 DIAG [117,119]	ELISA: 2 tested samples – 53-57%; 3 tested samples – 72%; ≥4 tested samples – 69%; 5 tested samples – 88%; 6 tested samples – 92%; ≥6 tested samples – 71% RT-PCR: 2 tested samples – 84%; 3 tested samples – >90%; 5 tested samples – 92%; 6 tested samples – 96%	High	-1	0	0	0	0	Moderate	
	Specificity*	1 DIAG [119]	ELISA: 2 to ≥6 samples – 100%	High	-1	0	0	-1	0	Low	

* These outcomes are considered the most critical by the guideline developers.
** These modifiers can impact the GRADE by 1 or 2 points

Q3: What patient interventions best prevent or contain norovirus outbreaks in the healthcare setting?

EVIDENCE TABLE Q3

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
Virus shedding						
Murata, T; 2007 [148]	Prospective controlled study 2,3,4	To describe children infected with norovirus and duration of viral shedding.	Children with acute gastroenteritis who presented to a pediatric clinic in Japan. Median age 18 months (range 3 months to 7 years). 71 (59 included for analysis)	**Symptoms** Vomiting 94.9% Diarrhea 94.9% Fever 20.3% **Severity of illness** Overall duration of illness – median 5 days *All results children <2 years old vs 2-5 years old; p value* Duration of illness in days – 7 vs. 3.5; 0.0069 Maximum number of stools – 7 vs. 3; 0.0078 20 point severity score developed for rotavirus – 11 vs. 8; 0.0031 **Period of viral shedding (n=26)** Overall in days – median, 16 (range, 5-47) Patients ≤6 months of age vs >1 year old in days – 42 vs. 10; p=0.0475 Shedding > 2 weeks in children <1 year vs. 1 year vs. 2-3 years of age – 6/8 (75%) vs. 5/7 (71.4%) vs. 2/8 (25%) Patients ≤6 months – 3/5 shed for long periods (42, 44, and >47 days)	Acute gastroenteritis was defined as the presence of either diarrhea or vomiting at presentation between November 1, 2002 to December 31, 2002. norovirus was diagnosed using RT-PCR. Power and sample size not reported.	176_IL
Rockx, B; 2002 [149]	Prospective controlled study (with a nested case control design) 1,3,4	To describe the natural history of CaCV infections in humans.	The case definition of gastroenteritis was ≥ 3 loose stools in 24 h, vomiting ≥ 3 times in 24 h, loose stools with two additional symptoms or vomiting with two additional symptoms. Additional symptoms included diarrhea, vomiting, nausea, fever, abdominal pain,	**Ages affected (until day 22 after the onset of symptoms)** Proportion of norovirus gastroenteritis cases was highest in children (age 0.5-17 yrs; proportion 14-19%) and elderly (age ≥ 65 yrs; proportion 13%) **Clinical symptoms** Clinical manifestations reported by 99 cases with norovirus infection were: Diarrhea – 87% Vomiting – 74% Abdominal pain – 51% Abdominal cramps – 44% Nausea – 49% Fever – 32% Mucus in stool – 19%	Clinical information was obtained from medical diaries kept by patients during the 4 weeks after the onset of symptoms. norovirus was detected by RT-PCR. Power and sample size not reported	934_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			abdominal cramps, and blood or mucus in stool. Healthy control subjects were selected for the same period and matched with cases by age and geographical location. Demographics not reported – community based population registered through the Netherlands Institute of Primary Health Care. Study conducted in Netherlands. 4860	Bloody stool – 0% **Median duration of symptoms (days)** Overall – 5 Age < 1 yr – 6 Age 1-4 yrs – 4 Age 5-11 yrs – 5 Age ≥ 12 yrs – 3 **Percentage of infected cases shedding virus** On day 1 – 78% On day 22 – 26% (Highest in newborns aged < 1 yr)		
Marshall, J; 2001 [150]	Descriptive study (Case report) N/A	To report a case excreting high levels of NLV in the absence of any clinical symptoms of gastroenteritis.	An elderly woman (71 yrs) who contracted norovirus infection during an outbreak in Australia 1	**Asymptomatic shedding** (day 2 and day 5 after resolution of symptoms) About 5 x 10^5 NLV virions per gram of feces were detected. These were closely related to Camberwell virus, a GII NLV	Stool specimens were analyzed using EM and RT-PCR	1056_RA
Hedlund, 1998; [151]	Descriptive study 1,2,3,4	To describe the role of NLV in pediatric diarrhea and describe asymptomatic shedding	All cases with stool samples positive for NLV 77 cases – 33 community acquired, 47 nosocomial	**Asymptomatic shedding** 5 of 17 children examined repeatedly excreted virus after the symptoms had subsided.	NLV identified by EM	3554_RA
Chiba, S; 1980 [152]	Descriptive study 1,3,4	To evaluate viral shedding and duration of illness.	Stool specimens were obtained from CaCV outbreaks in an orphanage in Sapporo, Japan.	**Stool specimens positive for CaCV** Overall – 29/61 (48%) *Symptomatic patients* *All results – positive/tested (%)* Obtained before onset of illness – 0/7 (0%)	Illness not defined	2140_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			61 stool samples.	Obtained within 4 days after onset of illness – 18/19 (95%) Obtained days 5-10 – 7/14 (50%) *Asymptomatic patients* *All results – positive/tested (%)* 3/10 (30%)		
Recovery of norovirus						
Dalling, J; 2004 [153]	Systematic review 1,2,3,7	To identify if environmental contamination contributes to prolonged or recurring outbreaks and to clarify appropriate terminal cleaning measures.	Search of Health Electronic Resources Online in Northern England (HEROINE). Databases included Books@Ovid, MyOvid@Hand, journals@OvidFullText, Cochrane Database of Systematic Reviews, American College of Physicians Journal Club, DARE and CCTR, Allied and Complementary Medicine (AMED), Cumulative Index Nursing and Allied Health, EMBASE, PREMEDLINE and MEDLINE (1996 to present), British Nursing Index, and the National Research Register. Websites included the Department of Health, Public Health Laboratory Service, CDC, Infection Control Nurses Association, and the World Health Organization.	**Transmission due to environmental contamination** Identified that environmental contamination occurred during outbreaks – 5/11 (55%) Environmental contamination considered cause of transmission – 9/11 (82%) Identified environmental contamination as cause of prolonged or recurring outbreaks – 0/11 (0%) **Environmental sampling** Identified environmental contamination – 3/5 studies 76/210 (36%) swabs positive from curtains, cushions, carpets, lockers, commodes, toilet rims, seats and handles, taps, basins, telephones, door handles, physiotherapy instrument handle, and horizontal surfaces above and below 1.5 meters including light fittings and mantelpieces. **Laboratory testing methods** Studies using RT-PCR – 100% Two studies recognized that RT-PCR positive for norovirus does not necessarily represent viable virus. **Sampling methods** *Methods of specimen collection* 3/5 studies used saline or transport medium moistened swabs for sampling; 0%, 31%, and 42% samples were positive. 1/5 studies used dry swabs; 0% samples were positive. 1/5 studies used wet and dry swabs; 13% samples were positive. There appeared to be more positive swabs in studies that used moistened swabs. *Timing of collection* Unclear in 3/5 studies whether swabs samples were collected before or after environmental cleaning. *Selection of sampling sites* 4/5 studies did not explain why certain sites were swabbed and did not identify total swabs taken from each site. **Virus survival**	Sample size and power not reported.	3958_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			Search terms included ("Norwalk" OR "norovirus" OR "Winter Vomiting" OR "Viral gastroenteritis" OR "SRSV" OR "Calicivirus") AND ("Outbreak" OR "Management" OR "Environment" OR "Disinfect" OR "Decontaminate" OR "Decontamination" OR "Clean" OR "Contaminate" OR "Contamination" OR "Precautions" OR "Control"). Limited to English language. Articles excluded if unrelated to viral gastroenteritis or environmental contamination; or focused on the source of infection (i.e., food borne gastroenteritis) or laboratory diagnosis techniques. References of articles reviewed to identify additional relevant articles. Articles critiqued using a tool adapted from Cormack. 11 articles. 5 articles included data from environmental	1 study reported 21-28 day survival in a dried state at room temperature. 2 studies reported virus survival for at least 12 days; 1 paper repeated sampling and did not find virus in a previously contaminated environment after 5 months. 1 study suggested that carpets may have viable virus for at least 12 days that is not removed by routine vacuum cleaning. **Changing curtains** 2 studies recommend changing curtains, but there is no evidence examining impact of curtain changes on duration or recurrence of outbreaks. **Carpet decontamination** 3 studies advised steam cleaning of carpets but there is no evidence examining impact of steam cleaning on norovirus survival. 1 study recommended steam cleaning carpets and changing curtains as Category II "strongly recommended and viewed as effective by experts in the field and by the working group, based on strong rationale and suggestive evidence, even though definitive studies may not have been done." 1 study identified carpets as a cleaning priority due to high levels of norovirus by RT-PCR. **Cleaning and disinfection** 4 studies recommended and/or performed terminal cleaning. 3 papers recommended a cleaning or disinfectant agent; all recommended hypochlorite 1000 ppm. Chadwick et al. recommendations based on Doultree et al. which recommended glutaraldehyde 0.5% and iodine 0.8%, but not 75% ethanol, quarternary ammonia 1:10 and anionic detergent 1%. Doultree et al. gives no reference for the recommendation. 2/5 studies that studied environmental sampling reported decontamination methods; both used 500 ppm hypochlorite, which is no longer advised in current guidelines. 0/5 studies evaluated the effectiveness of currently used disinfectants. **Specific areas for decontamination** 4 studies listed recommendations including decontamination of frequently handled objects, taps, door handles, toilets and bathrooms, bath rails, toys, carpets, and surfaces contaminated by stools or vomit. The only area recommended by > 1 study was bathrooms, despite 2 papers identifying by swabs contamination of both toilets and door handles.		

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			sampling.			
Wu, H; 2005 [154]	Prospective controlled study 1,3,4	To identify the likely mode of transmission, characterize risk factors for illness, and evaluate for environmental contamination in a norovirus outbreak.	Residents and employees of a long term care facility in Philadelphia. 97% residents were male, median age 77 yrs (range 40-103), 87% had a cardiovascular or chronic pulmonary condition, 28% had a gastrointestinal disorder, 24% had diabetes and 70% had organic brain disease, dementia or a psychiatric disorder. 246 residents and 246 employees	**Cases (follow up 41 days)** 127 residents and 84 employees met the case definition. **Transfer to acute care hospital (follow up 41 days)** *All results RR(95% CI) with non-case residents used as control* All case residents – 2.2(1.1-4.3) Case-residents during the early period – 1.7(0.8-3.5) Case-residents during the late period – 3.8(1.8-8.0) **Mortality (follow up 41 days)** *All results RR(95% CI) with non-case residents used as control* All case residents – 1.2(0.5-2.9) Case-residents during the early period – 1.0(0.4-2.5) Case-residents during the late period – 2.1(0.8-5.9) **Positive stool or vomitus samples (follow up 41 days)** All 8 stool samples and 1 of 3 vomitus samples from cases tested positive for norovirus **Environmental contamination (follow up 41 days)** **10 samples tested, 5 positive and match clinical sample genotype** Positive swabs – toilet seat, dining room table, elevator button, bed rail, toilet seat and hand rails Negative swabs – table, elevator button, handrail, wheelchair, bedrail, bedside table	Cases were defined as: three or more occurrences of loose stools in a 24 hr period OR one or more episodes of unexplained vomiting OR a physician diagnosis of acute gastroenteritis Stool/virus samples and environmental swabs were tested with RT-PCR 181 employees (74%) returned the surveys. "Early period" was defined as symptom onset before or during the peak of the outbreak, while "late period" was defined as after the early period Power and sample size not reported	406_RA
Jones, E; 2007 [155]	Descriptive study 1,2,3,4	To describe the role of fomite contamination during a norovirus outbreak	Participants in three consecutive 5-night educational boating trips. 36/54 were females. Study was conducted in Arizona, USA 54	**Positive fomites** Bathroom surfaces – 5/6 (83%) Kitchen surface samples – 2/5 (40%) Doorknob samples – 3/3 (100%) Samples of onboard potable water supplies were all negative	Random samples from interior boat surfaces and toilet reservoirs were collected by swabbing surfaces. norovirus was confirmed using RT-PCR. Stool samples were not available.	95_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
Clay, S; 2006 [156]	Descriptive Study 3	To assess the survival of FCV on fomites. FCV was used as a surrogate.	Fomites – keyboard keys, computer mouse, brass disks (as a representative for water faucets or door knobs), telephone buttons, telephone receiver and telephone wire. N/A	**Time to 90% reduction in viral titer (hrs) (follow up 144 hr)** Keyboard keys – 0 to 4 Computer mouse – 0 to 4 Brass – 0 to 4 Telephone buttons – 12 to 24 Telephone receiver – 4 to 8 Telephone wire – 0 to 4 **Time to undetectable virus (hrs) (follow up 144 hr)** Keyboard keys – 8 to12 Computer mouse – 24 to 48 Brass – 8 to 12 Telephone buttons – 48 to 72 Telephone receiver – 48 to 72 Telephone wire – 24 to 48		361_RA
Gallimore, C; 2006 [157]	Descriptive Study 1,3	To determine if gastroenteric viruses were present on surfaces and equipment. Environmental sampling was done using swabs and subsequent nucleic acid extraction and RT-PCR assays.	Swab sites in a pediatric primary immunodeficiency unit that were chosen to represent areas commonly in contact with hands. Three patients were also studied (two were patients with immunodeficiency < 1 month of age; one was a 4 yr old patient with lactose intolerance) 11 swab sites and 3 patients	**Environmental swabs positive for norovirus (every 2 weeks during a 6 month period)** *All results number of positive swabs/number of swabs taken for each swab site* Staff toilet door handle – 1/14 Staff toilet taps – 4/14 Telephone outside rooms 3 and 4 which contained the patients– 1/14 Microwave oven – 3/14 Room 4 outside flow syringe pump – 3/14 Room 3 outside flow syringe pump – 3/14 Parents' phone – 5/14 Parents' room door handle – 2/14 Game console – 1/14 Parents' toilet door handle – 1/14 Parents' toilet taps – 4/14 Recommendation: consider chlorine-based disinfectant for hard surfaces **norovirus detected in stool of patients with PCR (during a 6 month period)** norovirus was detected in the stool of 1 of the 3 patients		360_RA
Kuusi, M; 2002 [158]	Descriptive study 1	To conduct an epidemiological, environmental and virological investigation of an	Guests and staff at a rehabilitation center. Environmental samples were collected from water supply system, swimming pools, surfaces of 2	**Positive environmental samples (during ~1 month)** Ultrasound physiotherapy instrument's handle A bathroom door handle in a room of a symptomatic guest A toilet seat in a room of a symptomatic guest A toilet seat in a public toilet for women The environmental strain was identical to the strain detected from patient samples. Water	Detected using RT-PCR	914_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
		outbreak.	accommodation rooms with symptomatic guests, 2 sauna rooms, 2 bathrooms, 2 gym rooms, ultrasound treatment room, main entrance and restaurant. 280	samples and swimming pools were negative.		
Cheesbrough, J; 2000 [159]	Descriptive study 1,2,3,4	To investigate the pattern of norovirus contamination during and after an outbreak	Guests at a hotel in England. Demographic characteristics not reported. 144 environmental swabs	**Positive fomites during outbreak (61/144)** *All results positive fomites/total fomites; %* Carpet (known recent vomit) – 5/8; 62 *Carpet had been cleaned with detergent, water and then vacuumed prior to testing Carpet (no known recent vomit) – 9/12; 75 Toilet rims or seats – 8/11; 73 Toilet handles, taps, basins and surfaces – 13/33; 39 Horizontal surfaces (outside toilet) below 1.5 m, e.g. tables, ledges – 11/29; 37 Horizontal surfaces (outside toilet) above 1.5 m, e.g. mantle piece, light fittings – 6/12; 50 Frequently handled objects, phones, door handles – 7/29; 24 Soft furnishings, cushions, curtains, etc – 2/10; 20 **Post-outbreak follow-up** (5 months after outbreak) 0/144 positive samples	norovirus was confirmed by RT-PCR	1098_RA
Schvoerer, E; 1999 [160]	Descriptive study 3	To describe an outbreak of norovirus gastroenteritis	Patients at a re-education ward of a hospital in France. 6	**Symptoms** Nausea – 6/6 Vomiting – 2/6 Abdominal pain – 6/6 Fever – 2/6 **Positive water samples** 3/7 samples tested were positive for norovirus **Positive stool samples** 3/6 samples tested were positive for norovirus	norovirus was confirmed using RT-PCR on stool samples Outbreak was associated with contaminated drinking water	1280_RA
Green, J; 1998 [161]	Descriptive study 1,3	To describe a norovirus outbreak occurring in a hospital for the mentally ill	Patients and staff at a hospital for the mentally ill in the UK. The environmental sampling sites were all within dormitory 4, a	**Positive environmental samples** 11/36(27%) environmental swabs collected on the affected ward were positive for SRSV on day 3 of outbreak. The sites shown to be contaminated included lockers, curtains and commodes, all in proximity to symptomatic patients	norovirus in environmental samples was characterized using RT-PCR	1317_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			bay in which symptomatic patients were cohort nursed. 28 patients and staff; 36 environmental swabs			
Mattison, K; 2007 [112] Basic Science Study N/A	To assess virus survival in foods and on sufaces. FCV was used as a surrogate for norovirus to investigate its survival.	Food (lettuce, strawberry, ham) and metal surfaces. Study was conducted in Canada. N/A	**Survival of virus** *At 30 min* Lettuce – 20% Strawberry – 1% Ham – 43% Metal disk – 11% *At 7 days* There was a signifiant reduction in viral titer after 7 days for all samples at both room temperature (RT) and 4°C (P<0.05). **Comparison of virus survival at RT and 4°C (on day 7)** Lettuce – undetectable at RT; 1% survival at 4°C; statistical differences were not reported Strawberry – undetectable at both RT and 4°C; survived for 5 days at 4°C, compared with 1 day at RT; statistical differences were not reported Ham – P>0.05 Metal disk – P>0.05 **Comparison of virus survival among the different samples** The survival on ham was significantly greater when compared to all other surfaces at both temperatures (P<0.05)		154_RA
D'Souza, D; 2006 [162] Basic science study N/A	To investigate the stability of norovirus on various food preparation surfaces and to evaluate the degree of virus transfer from these surfaces to a model ready-to-eat food (lettuce).	Stainless steel, formica and ceramic coupons sterilized by autoclaving were used as the environmental surfaces N/A	**Detection of virus** *1. norovirus* Could be detected on all 3 surfaces for up to 7 days post inoculation *2. norovirus RNA* Not detected on stainless steel beyond 24 hrs. Data for the other surfaces not reported *3. FCV* Could be detected on all 3 surfaces for up to 7 days post inoculation, with 6-7 $\log_{10}$ drop in virus titer over the 7 day period. There were no significant differences in recovery between the three surfaces tested (P>0.05). Statistically significantly higher recovery at time point 0 (P<0.05), but virus recovery at 1, 2, 4, 8 and 24 hours not significantly different from each other (P>0.05). Virus recovery at 24 and 48 hrs not significantly different from each other (P>0.05). Virus recovery at 7 days significantly lower from prior time points (P<0.05).	Virus recovery was evaluated by RT-PCR (for norovirus and norovirus RNA) or by plaque assay (for FCV) using feline kidney cells	337_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
		Artificial contamination was done with: 1) norovirus, 2) norovirus RNA, or 3) FCV.		**Virus transfer between stainless steel surfaces** *All results are number of lettuce samples testing positive for norovirus at 10, 30 and 60 min virus drying time* Dry lettuce – 9/9; 0/9; 0/9 Wet lettuce – 8/9; 6/9; 7/9 Pressure applied to the samples did not have a statistically significant effect on transfer. Significantly higher transfer to wet lettuce (P<0.01). For dry lettuce, the transfer at time 0 was statistically significantly higher than at times 30 and 60 min (P<0.05). For wet lettuce, the transfer at time 0 was statistically significantly higher than at times 10, 30 and 60 min (P<0.05).		
Paulson, DS; 2005 [163]	Basic science	Current food code requires food handlers to wear gloves when handling ready-to-eat food. The study objective was to evaluate the amount of virus transferred from contaminated surfaces to gloved hands.	A simulation study was performed to determine the amount of virus transferred from contaminated stainless steel surfaces, spatulas, forks, cutting boards, door knobs, and lettuce to vinyl food handler gloves. Objects were inoculated with CaCV strain F9 viral suspension, and air dried for 5 or 15 minutes. A gloved fingertip was pressed lightly into the contaminated area for 5-10 seconds. The baseline viral load on the test items and the viral load recovered from gloved hands post-transfer were assessed.	**Virus transferred** *All results – Baseline; post-transfer recovery in virus log_{10} values* *5 minute dry time* Average baseline – 5.9; post-transfer recovery – 4.7-5.4 Spatula – 5.9 ± 0.23; 5.4 ± 0.03 Lettuce – 5.9 ± 0.23; 5.1 ± 0.20 Fork – 5.9 ± 0.23; 5.3 ± 0.15 Cutting board – 5.9 ± 0.23; 5.3 ± 0.13 Door knob – 5.9 ± 0.23; 4.7 ± 0.07 Stainless steel coupon – 5.9 ± 0.23; 5.2 ± 0.11 *15 minute dry time – All results virus log_{10} values* Average baseline – 5.8; post-transfer recovery – 4.9-5.3 Spatula – 5.8 ± 0.31; 5.3 ± 0.15 Lettuce – 5.8 ± 0.31; 5.3 ± 0.04 Fork – 5.8 ± 0.31; 5.2 ± 0.23 Cutting board – 5.8 ± 0.31; 5.2 ± 0.09 Door knob – 5.8 ± 0.31; 4.9 ± 0.18 Stainless steel coupon – 5.8 ± 0.31; 4.9 ± 0.13	As few as 10-100 viral particles may be sufficient to cause infection so there is definite risk for transmission by food handlers wearing gloves. Remaining questions: 1) How long can norovirus remain on inanimate surfaces and still be infectious and 2) how much virus is transferred from gloved hands to food?	4356_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
Components of an outbreak prevention/containment program						
Dalling, J; 2004 [153]	Systematic review 1,2,3,7	To identify if environmental contamination contributes to prolonged or recurring outbreaks and to clarify appropriate terminal cleaning measures.	Search of Health Electronic Resources Online in Northern England (HEROINE). Databases included Books@Ovid, MyOvid@Hand, journals@OvidFullText, , Cochrane Database of Systematic Reviews, American College of Physicians Journal Club, DARE and CCTR, Allied and Complementary Medicine, Cumulative Indsex Nursing and Allied Health, EMBASE, PREMEDLINE and MEDLINE (1996 to present), British Nursing Index, and the National Research Register. Websites included the Department of Health, Public Health Laboratory Service, CDC, Infection Control Nurses Association, and the World Health Organization. Search terms included ("Norwalk" OR "norovirus" OR "Winter Vomiting" OR "Viral gastroenteritis" OR	**Transmission due to environmental contamination** Identified that environmental contamination occurred during outbreaks – 5/11 (55%) Environmental contamination considered cause of transmission – 9/11 (82%) Identified environmental contamination as cause of prolonged or recurring outbreaks – 0% **Environmental sampling** Identified environmental contamination – 3/5 studies 76/210 (36%) swabs positive from curtains, cushions, carpets, lockers, commodes, toilet rims, seats and handles, taps, basins, telephones, door handles, physiotherapy instrument handle, and horizontal surfaces above and below 1.5 meters including light fittings and mantelpieces. **Laboratory testing methods** Studies using RT-PCR – 100% Two studies recognized that RT-PCR positive for norovirus does not necessarily represent viable virus. **Sampling methods** *Methods of specimen collection* 3 used saline or transport medium moistened swabs for sampling. 1 used dry swabs. 1 used wet and dry swabs. There were more positive swabs in studies that used moistened swabs. *Timing of collection* Unclear in 3 studies whether swabs were taken before or after environmental cleaning. *Selection of sampling sites* 4 studies did not explain why certain sites were swabbed and did not identify total swabs taken from each site. **Virus survival** 1 study reported 21-28 day survival in a dried state at room temperature. 2 studies reported virus survival for at least 12 days; 1 paper repeated sampling and did not find virus in a previously contaminated environment after 5 months. 1 paper suggested that carpets may have viable virus for at least 12 days that is not removed by routine vacuum cleaning. **Changing curtains** 2 studies recommend changing curtains, but there is no evidence addressing whether changing curtains would prolong an outbreak.	Sample size and power not reported.	3958_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			"SRSV" OR "Calicivirus") AND ("Outbreak" OR "Management" OR "Environment" OR "Disinfect" OR "Decontaminate" OR "Decontamination" OR "Clean" OR "Contaminate" OR "Contamination" OR "Precautions" OR "Control"). Limited to English language. Articles excluded if unrelated to viral gastroenteritis, environmental contamination, concentrated on the source of infection (i.e., food borne gastroenteritis), or laboratory diagnosis techniques. References of articles reviewed to identify additional relevant articles. Articles critiqued using a tool adapted from Cormack. 11 articles. 5 articles underwent environmental sampling.	**Carpet decontamination** 3 studies advised steam cleaning of carpets but there is no evidence that it is effective for norovirus. 1 study identified carpets as a cleaning priority due to high levels of RT-PCR. 1 study recommended steam cleaning carpets and changing curtains as Category II "strongly recommended and viewed as effective by experts in the field and by the working group, based on strong rationale and suggestive evidence, even though definitive studies may not have been done." **Cleaning and disinfection** 4 studies recommended and/or performed terminal cleaning. 3 papers recommended a cleaning or disinfectant agent; all recommended hypochlorite 1000 ppm. Chadwick recommendations based on Doultree article which recommended glutaraldehyde 0.5% and iodine 0.8%, but not 75% ethanol, quarternary ammonia 1:10 and anionic detergent 1%. The last study gives no reference for the recommendation. 2/5 studies that studied environmental sampling reported decontamination methods; both used 500 ppm hypochlorite, which is no longer advised in current guidelines. 0/5 studies evaluated the effectiveness of currently used disinfectants. **Specific areas for decontamination** 4 studies listed recommendations including decontamination of frequently handled objects, taps, door handles, toilets and bathrooms, bath rails, toys, carpets, and surfaces contaminated by stools or vomit. The only area recommended by > 1 study was bathrooms, despite 2 papers identifying contamination of both toilets and door handles by environmental swabs.		
MMWR; 2008 [79]	Prospective controlled study. 1,3,4	To investigate an outbreak at an elementary school.	Students and staff at an elementary school in Washington DC in February 2007.	**Risk factors for symptomatic illness** *Bivariate analysis: All results RR (95% CI); p value* Being a student – 0.94 (0.66-1.34); 0.76 Being female – 1.13 (0.82-1.56); 0.52	A case of gastrointestinal illness was defined as illness in a student or staff	017_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			Students – median age 8 years (range 3-12 years); 55% female. Staff – median age 41 years (range 13-66 years); 92% female. 266 – 207 students and 59 staff.	Having an ill contact – 1.76 (1.16-2.67); 0.01 Classroom J (first) – 1.94 (1.34-2.80); 0.02 Library use: 0.94 (0.58-1.52); 0.87 Library computer use: 1.08 (0.41-2.84); 1.00 **Interventionsrecommended** District of Columbia Department of Health recommended -more thorough handwashing with soap and water or alcohol-based hand sanitisers - cleaning all shared environmental surfaces with a diluted (1:50 concentration) household bleach -cleaning computer equipment (i.e., mice and keyboards) -excluding ill persons from school for at least 72 hours after resolution of illness	member with nausea, vomiting, or diarrhea, who was at the school February 2-18, 2007. Power and sample size not reported.	
Lopman, BA; 2004 [58]	Prospective controlled study 1,2,3,4	To describe norovirus outbreaks in residential homes or hospitals of principally older individuals.	Patients in hospitals and nursing homes in England. Cases were hospital patients, nursing home residents, and health care staff with ≥2 episodes of vomiting, ≥3 episodes of diarrhea, or both during a 24-hour period. Those with symptoms due to incontinence or ingestion of laxative drugs were excluded. 271 outbreaks – 33 in nursing homes and 238 in hospital units. 4378 cases – 2154 hospitalized patients, 1360 hospital care staff, 505 nursing home residents, and 358 nursing home staff.	**Duration of illness** Hospital patients vs. hospital staff, nursing home staff, and nursing home residents (75th percentile); p value – 3 days (5 days) vs. 2 days (3 days); p<0.001 Recovery was slowest in the oldest age group (≥85 years) of hospitalized patients - 40% symptomatic after 4 days	Outbreak is defined as ≥ 2 cases in a hospital functional care unit with dates of onset within 7 days of each other. Power and sample size not reported. Promotion of active surveillance (2-tiers of clinical symptoms) to detect cases as a means of prevention of outbreaks	642_IL
Lopman, B; 2004 [164]	Prospective controlled study 1,2,3,4	To identify and report costs of gastroenteritis	3 hospital systems in Avon, England. 2,154 patients and	**Attack rates** 2,154 patients – 2.21 cases/1,000 hospital-days (95% CI 2.16-2.25). 1,360 healthcare staff – 0.47 cases/1,000 hospital-days (95% CI 0.45-0.50). Attack rates for staff members lower than for patients: 19.6% (95% CI 16.6%-22.7%) vs	Outbreak defined as ≥ 2 cases in a functional care unit with dates of onset within 7 days of	592_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
		outbreaks in the UK from 2002 to 2003.	1,360 healthcare staff from 227 unit outbreaks.	46.8% (95% CI 40.9%-52.8%); p < 0.001. 227 unit outbreaks – 1.33 outbreaks/unit-year (95% CI 1.16-1.51). Units with outbreaks larger than those without outbreaks – 21.4 vs 12.6, p value < 0.0001. **Unit closure** Duration – mean 9.65 (95% CI 8.5-10.8) days; most extreme was a unit closed for 48 days. 3.57 (95% CI 1.86-5.2) bed-days lost for every day of unit closure. Estimated 5,443 bed-days lost from gastroenteritis outbreaks. **Costs** Empty beds – US $2.24 million or approximately $768,000/1,000 beds. Staff absence – $771,000 or $249,000/1,000 beds. Days of illness in working age men, women, and children – $106,000 or $36,000/1,000 beds. Bed-days lost plus staff absence – $3.15 million or $1.01 million/1,000 beds. By extrapolation, gastroenteritis outbreaks cost the English National Health Service US $184 million in one year (2002-2003). **Controlling outbreaks** Outbreaks contained faster when units rapidly closed to new admissions (within 4 days of the primary care): 7.9 vs 15.4 days; p=0.0023)	each other. Case was a patient or medical/nursing staff with vomiting (≥ 2 episodes of vomiting in a 24 hour period) OR diarrhea (≥ 3 loose stools in a 24 hour period) OR vomiting AND diarrhea (≥ 1 episodes of BOTH symptoms in a 24hour period) but excluding long standing diarrhea associated with disability or incontinence and diarrhea associated with laxative drugs. Costs derived from 1) bed-day loss from new admission restriction for affected units and 2) staff absence from illness. Unit Costs of Health and Social Care 2002 report used to estimate the economic loss from empty beds and staff absence. British pounds (2002) converted to US dollars at the rate of 1 pound: $1.6 based on the 5 year average 1999-2003. norovirus detected in 63% outbreaks:	

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
					confirmed etiologic agent in 61 outbreaks (50%) and detected in a single specimen in 16 outbreaks (13%).	
Billgren, M; 2002 [165]	Prospective controlled study 1,3,4	To describe outbreaks of norovirus gastroenteritis.	Ten hospitals representing 66% of the hospitals in Stockholm County., Sweden. These included medical and geriatric wards among others. Some medical and geriatric wards were randomly selected as controls. 211 wards	**Risk of an outbreak of norovirus gastroenteritis on a ward** Outbreak during the previous year (P<0.01) **Lessons learned** • Hospitals that applied stringent measures to viral spread such as avoiding transfer of patients and staff and emphasizing hygiene routines during the first week of a suspected outbreak could shorten and restrict the outbreak. In hospitals where these measures were introduced late, the outbreak spread to other wards. • It was not evident if other measures to any appreciable extent contributed to the shortening of the outbreaks. It was not obvious if measures such as keeping staff off duty until they had been asymptomatic for 48 h or closure to admission of new patients influenced the outcome of an outbreak.	The inclusion criteria for an outbreak were those of Kaplan in at least 3 persons during one week. Stool samples were analyzed using EM and RT-PCR Power and sample size not reported.	958_RA
Evans, M; 2002 [83]	Prospective controlled study 1,3,4	To describe an outbreak of norovirus gastroenteritis following vomiting by an attendee at a concert	Primary school children attending a concert at a metropolitan concert hall. Demographic characteristics not provided. 1229 children from 15 primary schools	**Description of outbreak** Following the vomiting, cleaning was done with an ordinary vacuum cleaner the following day. No hypochlorite based product was used. The index case was seated in tier 13. Several cases documented from exposure after initial concert, ie. index case not present but exposure continued **Auditorium seating as a risk factor for norovirus infection** (follow-up not clearly reported) Children seated in tiers 9-13 vs. children seated elsewhere – 199/387 vs. 58/797; RR(95% CI) = 7.1(5.4-9.2)	A case was defined as a person who had attended the concert hall and had developed vomiting and/or diarrhea within 24-72 hrs of the visit. NLV was confirmed in fecal samples using RT-PCR	897_RA
Lachlan, M; 2002 [84]	Prospective controlled study 1,3,4	To describe an outbreak of norovirus gastroenteritis and lessons learned.	Persons with a connection to a hotel linked to the outbreak or ill contacts of people who were unwell and had a connection with the hotel. 112 potentially exposed, 79 cases	**Symptomatic norovirus infection - Food specific attack rates** Beef sandwich – 1.35(1.08-1.67) Cheese sandwich – 1.33(1.06-1.67) Egg sandwich – 1.49(1.18-1.88) Ham sandwich – 1.39(1.14-1.69) Lamb sandwich – 1.46(1.28-1.66) Tuna sandwich – 1.27(1.02-1.60) Sausage sandwich – 1.01(0.77-1.32) Soup – 1.28(1.00-1.64), P<0.05 Parsley garnish – 0.71(0.18-2.83) Tomato garnish – 1.15(0.82-1.61) Hot chocolate – 1.45(1.28-1.65)	A case was defined as someone with symptoms of diarrhea, vomiting or abdominal pain or any combination of these more than once in 24 hours and a connection with the hotel where the outbreak started.	942_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Tea – 1.04(0.81-1.33) Coffee – 1.36(1.10-1.67) Ice – 1.25(1.00-1.57) Other drinks – 1.52(1.12-2.05) After applying a critical P value (<0.003) with Bonferroni correction, only egg sandwich and drinks from the bar (other drinks) were found to be statistically significant. **Lessons from the outbreak** 7. Outbreak control team meetings that are formally minuted with action points being highlighted on a flipchart 8. Good liaison with laboratory services to agree on clear pathways for the delivery and analysis of samples that became available during normal working hours or were processed over the weekend. 9. Rapid virological confirmation to reassure the public that appropriate control measures were in place and handle the media interest. 10. Joint visit to the outbreak premises by protective services and public health representatives to facilitate clear and open communication between all parties and secure a voluntary agreement from the hotel owner to cease all food preparation. 11. Food handlers should remain off work from onset of illness until 48 hours after diarrhea and vomiting have ceased 12. All those involved in carrying out interviews and analyzing data working from one site and through one computer network to improve the efficiency of working through contact lists, allowing rapid assessment of the epidemic curve and symptom pattern and the results of RR calculations of the foodstuffs.	norovirus was confirmed by EM	
Love, S; 2002 [85]	Prospective controlled study 1,3,4	To describe an outbreak of gastroenteritis and procedures implemented to control it.	Guests and employees of a Virginia hotel. There were 3 groups: Group A: Attendees of a business conference (n=110); median age of cases (n=34) 52 years; 59% cases female Group B: Physicians and their families (n=95); median age of cases (n=11) 31 years; 73% cases female Group C: Retired	**Risk factors for symptomatic norovirus infection** (follow-up unclear) Attending reception: RR(95% CI) – 2.1(1.1-4.0) Eating coleslaw at picnic: RR(95% CI) – 3.6(1.0-13.6) **Interventions** Infection control measures instituted: 5. Employees who were ill in the past two weeks or had an ill child in diapers were excluded from work for 1 day. Employees who were currently ill with vomiting or diarrhea were told not to work for 1 day after resolution of symptoms 6. All employees were instructed about hygiene and hand washing 5 days after initial cases 7. The facility was closed for 8 h to permit thorough cleaning of all food service areas and guest rooms. New guests were not accepted until all guestrooms, bathrooms, and common rooms were thoroughly cleaned 7 days after initial	A case was defined as vomiting or diarrhea in a hotel attendee or staff. norovirus confirmed by RT-PCR Power and sample size not reported.	915_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			persons (n=310); median age of cases (n=15) 71 years; 60% cases female 60 cases	cases 8. All cold food requiring hand-preparation was excluded from the menu. No open bowls of food such as chips or popcorn were served 7 days after initial cases **Response to intervention** (at two week follow-up) The hotel reported no further ill guests or employees		
Lo SV, 1994 [89]	Prospective controlled study 1,2,3,4	To investigate a SRSV gastroenteritis outbeak in 4 hospitals served by one central kitchen.	4 hospitals - 1 acute district general hospital and 3 smaller peripheral hospitals with long-stay and rehabilitation patients 81 patients and 114 staff in 4 hospitals Buffet lunch cohort study: n=41 completed quesionnaire Patient case-control study: 23/24 cases and 35/36 controls completed questionnaires. Staff case-control study: 22/27 cases and 49/54 controls completed questionnaire.	***Buffet lunch study n=41*** ***Food - RR (95% CI)*** Ham and tomato – RR 1.0 (0.6-1.7) Cheese and pickle – RR 0.8 (0.4-1.9) Turkey salad – RR 2.4 (1.4-4.1) Tuna – RR 1.2 (0.7-2.0) Sausage roll – RR 1.1 (0.6-1.8) Cheese and pineapple – RR 1.0 (0.6-1.8) Sausage mushroom – RR 1.6 (0.-2.9) Fresh fruit – RR 0.8 (0.3-2.3) Meringue – RR 0.9 (0.5-1.4) Orange juice – 1.0 (0.48-2.0) Wine – 1.0 (0.51-2.1) ***Patient case-control study n=23 cases and 35 controls*** ***Risk factor*** ***Food - OR (95% CI)*** March 7th Beel cobble – OR 0 (0-1.7) Beef crumble – OR 1.6 (0-11.5) Mince – OR 0.7 (0.1-3.9) Sausage and onion – OR 0.3 (0.1-1.3) Cheese pie – OR 0.2 (0-1.6) Lamb salad – OR 0.4 (0.05-2.4) Tuna salad – OR 6.6 (1.0-71.6); p<0.05 Any salad – OR 1.8 (0.5-6.8) Corn beef sandwich – OR 1.6 (0.1-23) Any sandwich OR 4.6 (0.6-39) March 8th Cod – OR 1 (0.3-3.5) Chicken curry – OR 0.8 (0.2-2.8) Flaked fish – OR 0.7 (0.01-15) Lamb casserole – OR 0.9 (0.2-3.9) Mushroom pizza – OR 0.3 (0.01-3.9)	A cohort study of staff who attended a retirement buffet lunch, a patient case-control study based at the district general hospital, and a nursing staff case-control study at the district general hospital were performed. Fecal samples underwent bacteriological examination, routine EM, and immuno-EM. Power and sample size not reported.	1540_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Savoury lamb – OR 1 (0.1-9.7) Beef salad – OR 3.2 (0.2-97) Chicken salad – OR 2.5 (0.3-31) Any salad – OR 4.7 (0.9-30); p <0.05 Salmon sandwich – OR 0.2 (0-2.2) Any sandwich – OR 0.4 (0.04-2.3) March 9th Pork casserole - OR 1.5 (0.4-5.7) Chicken pie – OR 0.3 (0.1-1.5) Minced chicken – OR 0.2 (0-1.6) Cawl – OR 1.6 (0.2-13) Fishcake – OR 0.5 (0.1-2.5) Egg salad – OR 0.3 (0-3.9) Cheese salad – OR 2.2 (0.2-4.8) Any salad – OR 1.1 (0.2-4.8) Ham sandwich – OR 0.5 (0.01-6.7) Any sandwich – OR 1 (0.1-9.7) ***Staff case-control study*** No statistically significant associations found. 1 food handler who prepared the salad had a child who was ill 2 days prior and the food handler became ill the day following food preparation. ***Infection control practices*** Closure of the central kitchen Disposal of all remaining food Discontinuing all hospital admissions and ward transfers Daily ward cleaning with 2% hypochlorite Emphasis on hand washing		
de Wit, M; 2007 [92]	Retrospective controlled study 1,3,4,6,7	To describe an outbreak of gastroenteritis caused by a baker infected with norovirus who continued to work in his bakery having washed his hands and	Staff of a department in the Netherlands who attended a reception where the outbreak was reported. Median age 39 years; 45% female. 800-900 employees; 231 reported diarrhea or vomiting	**Symptoms** Diarrhea and vomiting – 76% Diarrhea only – 12% Vomiting only – 12% Median time to onset of symptoms – 31 hours **Risk factors for symptomatic infection** *All results OR(95% CI)* *Univariate analysis* Coffee – 0.3(0.1-0.9) Tea – 0.7(0.2-2.0)	A case was defined as a member of the departmental staff who attended the reception and reported diarrhea (3 or more loose stools a day) or vomiting in the 72 hours following the reception. A control was defined as a member of the	4084_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
		disinfected countertops.		Milk – 1.3(0.9-1.9) Butter milk – 1.1(0.7-1.8) Orange juice – 1.2(0.8-1.6) Champagne – 1.6(1.1-2.3) Cheese – 1.5(1.1-2.2) Brie – 1.1(0.7-1.8) Ham – 1.5(1.0-2.2) Beef – 1.2(0.8-1.9) Tuna salad – 1.6(1.1-2.4) Salmon salad – 2.2(1.0-4.5) Egg salad – 1.4(0.9-2.1) Raisin roll – 0.9(0.6-1.3) Increasing number of rolls – 2.0(1.6-2.4) *Multivariate analysis* Coffee – 0.4(0.1-0.8) Raisin roll – 0.5(0.3-0.8) Number of rolls – 2.0(1.5-2.5) **Intervention implemented** Sick food handlers excluded from work for 48hrs and reinforcement of hygiene measures	department staff attending the reception without diarrhea or vomiting in the 72 hours following the reception. norovirus infection was confirmed using RT-PCR The estimated response rate for questionnaires among cases was nearly 100%. The estimated response rate among controls was 40-50% Power and sample size not reported	
Hansen, S; 2007 [166]	Retrospective controlled study 1,3,4	To perform a systematic analysis of when ward closure was needed.	The Outbreak Database, which includes approximately 75% of all nosocomial outbreaks published in PubMed, was searched to identify how many outbreaks required closure. 1561 outbreaks	**Closure rates by ward** Overall – 194/1561 (12.4%) *All results – No. outbreaks with closure/No. outbreaks (rates); p value* General surgery – 44/346 (12.7%); NS Neonatology – 53/332 (16.0%); NS Internal medicine – 44/307 (14.3%); NS Pediatric ward – 8/132 (6.1%); 0.03 Hematology/oncology – 12/125 (9.6%); NS Geriatrics – 24/79 (30.3%); <0.001 General medicine – 3/76 (3.9%); 0.03 Hemodialysis – 5/76 (6.6%); NS Neurology/psychiatry – 7/66 (10.6%); NS Gynecology/obstetrics – 10/58 (17.2%); NS Transplantation units – 5/56 (8.9%); NS Orthopedics – 9/40 (22.5%); NS Neurosurgery – 9/39 (17.9%); 0.05 Urology – 5/38 (13.2%); NS **Closure rates by pathogen** *All results – No. outbreaks with closure/No. outbreaks (rates); p value*	Any partial or total closure of an affected location for any duration included. Each closure rate compared to the overall closure rate. Power and sample size not reported.	141_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				S. aureus – 23/223 (10.3%); NS Hepatitis virus – 6/150 (4.0%); 0.002 Pseudomonas spp – 10/130 (7.7%); NS Klebsiella spp – 10/115 (8.7%); NS Acinetobacter spp – 24/105 (22.9%); 0.02 Serratia spp – 14/94 (14.9%); NS Enterococci – 8/67 (11.9%); NS Enterobacter spp – 10/66 (15.2%); NS Streptococci – 19/63 (28.6%); 0.001 Salmonella spp – 4/56 (7.1%); NS Legionella spp – 2/48 (4.2%); NS norovirus – 15/34 (44.1%); <0.001 Clostridium spp – 4/34 (11.8%); NS Aspergillus spp – 5/25 (20.05%); NS Influenza/parainfluenza virus – 10/26 (38.5%); <0.001 Citrobacter spp – 3/12 (25.0%); NS Adenovirus – 3/11 (27.3%); NS Shigella spp – 4/11 (36.4%); 0.04 Rotavirus – 7/27 (25.9%); 0.05 SARS – 4/12 (33.3%); NS **Closure rates by source of outbreak** *All results – No. outbreaks with closure/No. outbreaks (rates); p value* Patient – 66/395 (16.7%); 0.03 Environment – 24/194 (12.4%); NS Medical devices – 12/172 (7.0%); 0.04 Personnel – 17/154 (11.0%); NS Drugs – 3/73 (4.1%); 0.03 Food – 1/50 (2.0%); 0.03 Equipment for patient care – 5/35 (14.3%); NS Source not known – 80/518 (13.8%); NS **Closure rates by route of transmission** *All results – No. outbreaks with closure/No. outbreaks (rates); p value* Contact – 124/752 (16.5%); 0.01 Invasive techniques – 13/273 (4.8%); 0.01 Inhalation – 31/166 (18.7%); 0.02 Ingestions – 4/63 (6.3%); NS Mode not known – 41/404 (10.1%); NS **Closure rates by type of infection**		

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				All results – No. outbreaks with closure/No. outbreaks (rates); p value Bloodstream infections – 76/589 (12.9%); NS Gastrointestinal tract – 49/402 (12.2%); NS Pneumonia – 44/331 (13.3%); NS Surgical site infection – 21/195 (10.7%); NS Urinary tract – 23/190 (12.1%); NS Skin and soft tissue – 21/171 (12.3%); NS Other lower respiratory tract – 21/134 (15.7%); NS ENT – 24/109 (22.0%); 0.004 CNS – 23/95 (24.2%); 0.001 Other systemic infections – 7/49 (14.3%); NS Bones and joints – 5/44 (11.4%); NS Cardiovascular system – 4/34 (11.8%); NS **Duration** Duration of closure described in 32 outbreaks – median, 14 days (range, 3-56). **Interventions for all outbreaks, not limited to norovirus** -Closure of entire unit (69.6%) -Infected or colonized patients isolated (66%) -Patient screening cultures and surveillance (58%) -Staff screening cultures and surveillance (49.5%) -Enforced hand hygiene (43.3%) -Reprocessing of devices (43.3%) -Healthcare worker education (24.2%) -Work load restriction (16.5%) -Vaccination (4.7%)		
Zingg, W; 2005 [167]	Retrospective controlled study 1,2,3,4,6,7	To describe a nosocomial norovirus outbreak, its management, and financial impact.	Patients at a Swiss university hospital. Age – mean 57.8 years. Sex – 56% male 16 case patients and 32 control patients.	**Symptomatic infection - Attack rate** 29.5%. **Costs** Overall – $40,675 *Laboratory testing* $2707 for laboratory tests (13 tested, 3 based on clinical symptoms) *Loss of revenue due to bed closures* $37,968 *Median numbers of occupied beds: Outbreak vs other non-outbreak periods* 29 beds/day in 2003 vs 42 beds/day in 2001, 43 beds/day in 2002, 42.5 beds/day (p=0.002, Mann-Whitney U test). Differences in median bed occupancy between peak incidence of illness and periods	Case was a patient or healthcare worker who developed acute diarrhea, nausea, and vomiting during the outbreak period; and had norovirus detected by RT-PCR in stool specimens. (12 definite cases; 3 probable cases with typical symptoms but not tested; and 1 with typical symptoms but	521_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				preceding and following (p<0.01). **Costs not included** *Nursing care* $10,300 (based on additional nursing care, in minutes) *Nursing care for case vs control patients – All results in median minutes/day; p value* Total – 74.3 vs 41.9; <0.05 Mobilization care – 105 vs 30; 0.05 Control of excretions – 202 vs 127.5; .54 Instructions – 30 vs 30; .42 Isolation measures – 180 vs 0;<0.0001 Difference due to need for isolation of infected cases (median, 180 minutes/day). *Lost productivity costs due to healthcare worker on sick leave* $12,807. *Infection control* $1408 **Interventions** -Infected patients isolated until 2 days after diarrhea resolved. -Gloves and gowns during direct patient contact until 2 days after the diarrhea resolved. -No new patient admissions or transfers. -Hand antisepsis and hand washing. -Rooms decontaminated with 0.5% hypochlorite after patient discharge. -Infected healthcare workers stayed home and were allowed to return to work 2 days after symptoms resolved. These measures did not completely prevent new cases, but there was a decrease in the incidence of new cases after these measures were implemented.	norovirus RT-PCR negative.) Control was a patient hospitalized during the outbreak on the same medicine ward without symptoms of gastroenteritis, matched by age, sex, underlying disease category, and length of stay. Power and sample size not reported.	
Oppermann, H; 2001 [63]	Retrospective controlled study 1,2,3,4	To identify risk factors for a gastroenteritis outbreak.	Guests and staff at a mother and child health clinic in Germany. Cases –166 guests and 49 staff. Data available – 164 guests and 47 staff.	**Symptomatic infection - Attack Rates** Guests 44% - adults 27% and children 54% Staff 23.4% **Age** *All results affected vs. not affected in years; p value* Children – 3.5 vs 6.3; <0.001 Adults – 32 vs 33; NS **Lessions Learned** **-Importance of early recognition of norovirus infection**	Case was a person who stayed at the health clinic from October 27 to November 17, 1999 and had vomiting and/or diarrhea at earliest, one day after his/her arrival. NLV and Astroviruses	1041_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Guests encouraged to wash hands after using the bathroom and prior to each meal. -Patients informed doctors immediately of any gastrointestinal symptoms. -Infected persons had limited contact with other guests and limited use of common facilities. -The staff was told immediately when gastroenteritis reported and instructed about appropriate protective measures. -The rooms of the infected persons, especially lavatories, were cleaned daily using a virucidal disinfectant. -Height of tables raised to prevent children from touching food -Newly arrived guests received meals in separate area from exposed guests -Vomitus disinfected immediately. -If an outbreak suspected, the public health department was to be notified.	detected using PCR. Power and sample size not reported.	
Marx, A; 1999 [66]	Retrospective controlled study 1,3,4	To assess risk factors for gastroenteritis associated with Norwalk-like viruses (NLVs)	Residents and employees at a geriatric long term care facility. 68% residents were female, median age was 83 yrs (range 65-106). 78% of employees were female, median age was 36 yrs. Study was conducted in Washington State. 91 residents and 97 employees	**Attack rate** Residents – 52/91 (57%) Employees – 34/90 (35%) *All results RR(95% CI); P value for the presence of risk factor* **Risk factors for gastroenteritis among residents** Physical dependence – 3.5(1.0-12.9);0.02 Respiratory therapy – 2.3(0.8-6.4); 0.20 Antibiotics – 1.6(1.0-2.8); 0.20 Chronic infections – 1.6(0.9-3.0); 0.40 Tube feeding – 1.3(0.7-2.6); 0.70 Disoriented – 1.2(0.8-1.8); 0.60 Diuretics – 0.4(0.2-0.9); 0.02 **Risk factors for gastroenteritis among employees** Exposure to vomitus – 2.6(1.1-6.5); 0.03 Gastroenteritis in household – 2.3(1.4-3.6); 0.01 Exposure to residents with gastroenteritis – 2.2(1.0-4.9); 0.05 Resident care – 1.4(0.8-2.5); 0.30 Tap water – 0.9(0.5-1.5); 0.60 Ice – 0.7(0.4-1.2); 0.20 **Effect of protective measures among nursing staff** Gowning – 0.4(0.1-1.4) Strict hand washing – 0.7(0.2-1.3) Use of hand-disinfection gel – 0.8(0.4-1.4) Laundering work clothes daily – 1.2(0.7-1.3)	A case of acute gastroenteritis was defined as an individual with onset of vomiting or diarrhea during the study period (Feb 12 – Mar 20 1996); diarrhea was defined as ≥2 loose or watery stools in a 24 hr period. A single NLV strain of genogroup II genetically related to Toronto virus was the only pathogen identified. NLVs were identified by EM in stool and vomitus specimens and further characterized by RT-PCR and nucleotide sequencing. Data on residents was collected through medical records. 90 of 97 employees completed a self-administered	1237_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
					questionnaire Power and sample size not reported	
McEvoy, M; 1996 [102]	Retrospective controlled study 1,3,4	To describe an outbreak of norovirus gastroenteritis.	Passengers and crew of 4 cruises in the western Mediterranean. Median age of cases 55 years; 13/23 males 46 (23 cases and 23 controls)	**Risk factors for symptomatic norovirus infection** (matched pairs analysis) *All results OR; P value* Gala dinner – 0.20; 0.22 Salad – 1.00; 0.77 Fruit – 0.56; 0.42 Eggs – 0.50; 0.38 Table – 1.33; 1.00 Taps – OR not calculable; 0.24 Ice (tap water) – 0.56; 0.42 Teeth (tap water) – 1.00; 0.77 Pool – 0.71; 0.77 Chicken – 0.50; 0.39 Prawns – 0.29; 0.18 Meat – 1.14; 1.00 Cream – 0.67; 0.75 **Interventions** 4. Hygiene measures were introduced in the galley 5. When the passengers disembarked for a short period, the cabins were cleaned with a chlorine based disinfectant 6. Soft furnishings were removed for steam cleaning from all cabins whose occupants had reported illness. At the same time, the crew and staff quarters, including communal bathrooms and lavatories, were cleaned in the same way. **Response to outbreak** After control measures were implemented, fewer than 10 cases of diarrhea and/or vomiting were detected on each of the fifth and sixth cruises	A primary cabin case (the first case to have occurred in a cabin) was defined as a passenger on the ship from 27 May to 2 June with diarrhea (≥3 loose stools in a 24 hour period) and/or vomiting. Controls were matched to cases by sex and age (within 10 years) norovirus was identified by EM and RT-PCR in fecal specimens 277/1100 questionnaires were completed and returned. Power and sample size not reported.	1410_RA
Chadwick, PR; 1994 [103]	Retrospective controlled study 1,3,4,6,7	To determine risk factors for small round structured virus infection during an outbreak at an elderly care unit.	Healthcare workers at an elderly care unit. Cases – mean age 36 years (range 21-58 years). Controls – mean age 39 years (range 18-59 years). 90% questionnaire responders were	**Clinical features** Overall attack rate – 34% *Attack rates among healthcare subspecialties* Nursing – 40% Pharmacists – 34% Doctors – 0% Staff absent from work due to illness – 75% Duration of absence – median 2 days (range 1-9 days)	Case was a patient or staff at the hospital with vomiting or ≥2 loose stools in a 24 hour period. Power and sample size not reported. Aerosolization of vomit	1555_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			female. 103 questionnaires returned.	**Risk factors for symptomatic infection** *Univariate analysis* Nearby vomiting – 50% exposed staff were infected vs. 20% unexposed staff; OR 3.89 (95% CI 1.4-11); p=0.007 Number of exposures to nearby vomiting – p=0.032 Contact with ill patients – 42% exposed staff were infected vs. 13% unexposed staff; OR 4.71 (95% CI 0.94-46); p=0.07 Number of close contacts with ill patients – p=0.023 Cleaning vomit – OR 1.96 (95% CI 0.46-9.8); p=0.49 Cleaning diarrhea – OR 4.67 (96% CI 0.49-225); p=0.22 *Multivariate analysis* Nearby vomiting was the only significant risk factor **Interventions Implemented** Handwashing emphasized Restricted transfers from affected wards Ward closures Staff cohorting Disinfection with chlorine-based products Attribute declining attack rates among subsequent wards to infection control measures	may have been important in infection transmission during the outbreak. Exposure to nearby vomiting defined as vomiting occurring within 6 feet of the health care worker.	
Johnston, CP; 2007 [168]	Descriptive study 1,2,3,4	To describe a norovirus outbreak	Patients and staff in coronary care and psychiatric units in a tertiary care hospital.. 355 cases – 90 patients and 265 health care workers Mean ages ± SD years – healthcare workers 36.2 ± 10.4 and patients 45.5 ± 23.4. Female – 83.8% healthcare workers and 47.8% patients.	**Descriptive** *Attack rates* Cardiac/coronary care unit (CCU) – 7/133 (5.3%) for patients and 29/97 (29.9%) for health care workers. Psychiatry unit – 39/233 (16.7%) for patients and 76/200 (38.0%) for health care workers. CCU - Employees used a total of 138 hours of sick leave and 18.5 hours of overtime. Psychiatry units – Despite routine infection control measures, additional cases occurred. **Costs** (US$) *Lost revenue* CCU – $147,507 Cardiac/coronary intensitve care unit (CICU) – $158,620 Psychiatry – $112, 242 *Additional costs* Cleaning – $96,961 Replacement of supplies – $53,075 Sick leave and overtime – $89,239	Cases were those with new onset vomiting and/or diarrhea during the outbreak period. Diarrhea was defined as ≥ 2 loose stools/24 hour period or unexplained increase in bowel movements. Norovirus genogroup II-4 variant detected. Economic analysis focused on the institutional costs of the outbreak from the Johns Hopkins Hospital Casemix	079_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Total – $657,644 **Interventions** *At initial outbreak* -Healthcare workers educated on how to identify norovirus gastroenteritis, appropriate cleaning measures, and isolation protocols. -Infected healthcare workers returned to work 72 hours after symptom resolution. -Standard precautions and Contact Precautions of symptomatic patients. -Symptomatic patients in private rooms or cohorted together. -In the emergency room, symptomatic patients cohorted together. -Frequent hand hygiene with either soap and water or alcohol based hand gel encouraged. -Healthcare workers at other institutions not allowed to care for patients at this institution (outbreak was citywide). -Closure of emergency department at a nearby hospital that had a gastroenteritis outbreak – the outbreak affected the entire city. -Nurse managers and infection control professionals screened patients and healthcare workers daily, reinforcing infection control practices. -Nurse managers screened all visitors for gastroenteritis, and if symptomatic, prohibited them from visiting patients in the units for 72 hours. -Sharing of food among healthcare workers was prohibited. -Aggressive cleaning measures implemented using 1:50 dilution of sodium hypochlorite (i.e., bleach). -Every shift, high touch surfaces (i.e., doorknobs, light switches, tables, counter tops, computer keyboards), and bathrooms (particularly toilets and fixtures) cleaned. -Daily, patient rooms (including walls, windows, beds, chairs, and ledges) cleaned; rooms of patients who vomited or had diarrhea were cleaned last. Floors were cleaned, replacing cleaning solutions and mop heads every 3 rooms. -At discharge, patient rooms, floors, patient dressers and overbed tables cleaned. Room contents were discarded, the room cleaned, and then restocked. -Surfaces soiled or grossly contaminated were cleaned, and curtains changed. *Additional interventions when additional cases identified (implemented 3 days after initial interventions)* -Visitors prohibited, unless extenuating circumstances. -Nurses on affected floors cohorted – one group cared for symptomatic patients and a second group for asymptomatic patients. -Gowns and gloves used until outbreak resolved. -No new admissions in several units because of staffing shortages. -CCU closed for 24 hours while extensive cleaning occurred. -All disposable supplies, including medical supplies, discarded.	administrative database. Costs included total lost revenue with closure of units to new admissions, attributable sick leave and overtime salary, cost of replacing supplies, and cleaning expenses. Analysis limited to CICU, psychiatry units, and echocardiogram laboratory. Power and sample size not reported.	

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				-Items with fabric surfaces, including furniture, that could not be disinfected were discarded. -All surfaces cleaned with sodium hypochlorite by two consecutive cleaning crews. -In the psychiatric unit, group sessions suspended and patients with gastroenteritis confined to their rooms and limited transport of patients to other hospital areas (implemented >1 month after initial interventions on psychiatric ward)		
Leuenberger S; 2007 [169]	Descriptive study 1,2	To describe a norovirus outbreak in a Swiss hospital.	Patients in the geriatric and internal medicine wards where two outbreaks occurred. 77 persons in 2 buildings – 28 patients and 49 healthcare workers – 39 in building 1 including the geriatric ward and 38 in building 2, including the internal medicine, intensive care, surgery, orthopedic, and obstetrics and gynecology wards	**Interventions** -Public restaurant in building 1 closed due to an infected staff member. -Infected healthcare workers sent home for at least 48 hours. -Infected patients isolated and cohorted. -Movement of infected patients minimized. -Healthcare workers and visitors wore masks, gloves, and gowns. -Mandatory hand disinfection with a product that has 95% ethanol. -Daily surface disinfection.	Case was someone with sudden vomiting and diarrhea, abdominal cramps, fever below 38.5°C, and recovery within 48 hours. 4/18 samples tested positive for norovirus genogroup II cluster 4. Diagostic testing could not link the two outbreaks. The authors speculated that the large outbreak resulted from a more virulent and environmentally stable norovirus strain.	163_IL
Cheng, F; 2006 [170]	Descriptive study 1,2,3	To provide a practical action plan for effective infection control of a norovirus outbreak in acute pediatric wards	Patients, parents, visitors, health care workers or medical students who developed vomiting or diarrhea and were exposed to inpatients of a pediatric ward within four days of an outbreak. The setting was a university hospital in Hong Kong.	**Interventions** *1. Isolation of infected patients.* • Alert the hospital infection control team if ≥3 inpatients developed gastroenteritis after admission. • Cohort and isolate all symptomatic cases. • Patients exposed but remaining asymptomatic should stay in the original ward and should only be isolated if they develop clinical symptoms. • Stop admitting new patients to the ward in a suspected outbreak. *2. Disease surveillance and contact tracing.* • Define the surveillance period (e.g. four days before the onset of presentation of the index case for a suspected norovirus outbreak). • Establish a case definition for the outbreak.	Diarrhea was defined as changing from well-formed stool to ≥3 episodes of loose stools per day. Stool and rectal swab samples were evaluated using RT-PCR	282_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			There were 11 subjects, including 9 patients, 1 visitor and 1 medical student. Of these 6 were females and 5 were males. Age 4 mos. to 22 yrs	• Active surveillance and case finding for symptomatic inpatients. • Contact tracing of symptomatic cases among medical, nursing and allied health workers, and reviewing sick leave record of hospital staff. • Review admission records for phone contacts to trace symptomatic patients already discharged from the ward, and their parents and visitors. • Inform the University Health Service to trace medical students participating in the pediatric clerkship. *3. Infection control measures.* • Stringent contact precautions. • Enforce stringent hand hygiene policy in all pediatric wards. • Wear gloves, surgical masks and disposable plastic gowns when in contact with symptomatic patients or contaminated environment. • Remove toys and magazines displayed in the ward. *4. Environmental cleansing.* • Use concentrated disinfectant (hypochlorite solution 1000 ppm) for environmental cleansing. • Increase the frequency of routine cleansing in the ward (e.g. twice daily). • Widen the cleansing area to one square meter surrounding the contaminated area *5. Visiting policy* • Register all visitors and keep records for 14 days. • Restrict the number of visitors to two (i.e. parents only) for each inpatient. • All visitors should be screened by a standard questionnaire for symptoms and signs of gastroenteritis. *6. Staff management.* • Essential medical and paramedical staff who worked in affected ward were not allowed to work in unaffected clinical areas. • Non-essential personnel should not be allowed to enter the affected ward. • Symptomatic staff should discontinue clinical duties and seek medical advice immediately. *7. Others* • Posters about hand hygiene should be shown at the entrance of the ward. • Departmental seminars to educate staff on proper infection control measures and the clinical features of norovirus gastroenteritis. **Impact of Interventions** The outbreak was terminated within 3 days after the implementation of the infection control measures		
Simon, A; 2006 [171]	Descriptive study	To describe a norovirus	Patients of a pediatric oncology unit in	**Outbreak description** 28.9% stool specimens tested positive for norovirus. Outbreak stopped with the start of	All tool samples tested with RT-PCR	306_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
	1,2,3	outbreak.	Germany. 14 males, 6 females. Median age 43 months (range 4-288 mos) 20 patients (11 outbreak, 9 sporadic) and 2 relatives	the interventions **Viral shedding** Median (Range) in days – 23(3-140) among 12 patients with >2 positive results who underwent weekly testing **Interventions** 1. Hand hygiene with 95% ethanol 2. Use of masks when in close contact with symptomatic patients 3. All patients were tested for norovirus and were isolated in cohorts if positive	Viral shedding was defined as positive RT-PCR Nosocomial cases were identified as those with start of symptoms at least 24 hours after hospitalization	
Conway, R; 2005 [172]	Descriptive study None	To describe the management of an outbreak of norovirus.	Patients and staff at a tertiary care hospital. Demographic characteristics were not reported Sample size not reported	**Interventions** 1. Patients with loose or watery stools were reported to the Nursing Unit Manager or clinical coordinator for investigation. 2. Stool specimens or rectal swabs were collected on all patients. 3. Three wards managed the at-risk patients and patients who tested positive for norovirus during the outbreak. Patients were relocated and isolated from other patients, visitors and staff. 4. Barriers and signs were used to indicate entry and exit points for the isolated areas. 5. Dedicated nursing staff were allocated to care for these patients and skill mix and number of staff was assessed and allocated on a daily basis. 6. Nursing staff allocated to the care of these cohorts of patients were required to wear surgical scrubs, which were changed when leaving the ward. Any staff member entering the isolated area wore a disposable gown and gloves. 7. When dealing with explosive feces or projectile vomiting, a P2/N95 mask was worn to prevent staff from being affected by the aerosolization. 8. Upon leaving the isolated area all gowns, gloves and masks were disposed of and strict hand washing was enforced. 9. The Nursing Unit Manager assessed the cohorts of patients on a daily basis and provided an updated list. 10. Any patients who were symptom free for 48 hours were removed from the cohort and transferred to another area of the hospital. If cohort patients were being transferred to another facility, their discharges were delayed until the patients were symptom free for 48 hours. 11. Each ward involved in outbreak management was closed to any new admissions or transfers during the peak of the outbreak. To limit exposure to the outbreak, visitors were limited to only the immediate family. Children and elderly visitors were discouraged from visiting. 12. Education was provided to family members. 13. Disposable crockery and cutlery were arranged for the cohorts and kitchen staff	Cases were patients with loose or watery stools. norovirus confirmed using RT-PCR	3894_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				were not permitted to enter the areas. The cleaning process in the kitchen was assessed and met the standard for cleaning the meal trays. 14. Affected staff members were advised to exclude themselves from work until symptom-free for 48 hours		
Cooper, E; 2005 [205]	Descriptive study 1,2,3	To describe a norovirus outbreak at a long term care facility.	Patients and staff on 3 wards in a 500 bed long term care facility in Australia. 52 patients and 11 staff.	**Interventions** The infection control team implemented the following measures consistent with the Victoria Department of Human Services guideline "Controlling an Outbreak of Gastroenteritis: Guidance for Institutions": -No patient transfers between wards or to other institutions. -Infected patients cohorted. -Hand hygiene encouraged and alcohol-based handrubs available by every bedside. -Gowns and gloves worn. -Detergent and water, followed by a 1,000-ppm solution of sodium hypochlorite used for cleaning. -Wards closed to new admissions. -Staff only scheduled to the same ward. -Visiting restricted. -Exposed food discarded. -Staff educated about how gastroenteritis spread, cleaning and disinfection procedures, isolation, transfers, and discharge. -Infected staff could not return to work until 48 hours after symptom resolution. -Contact information for the infection control team made available. The outbreak ended 32 days after the first symptoms of acute gastroenteritis identified.	norovirus genotype 2 detected on 2 of 3 wards. Power and sample size not reported.	5586_IL
Navarro, G; 2005 [174]	Descriptive study 1,2,3,4	To describe an outbreak in a long-term care unit in Spain.	Patients, residents, and staff in a long term care hospital in Spain. 82% female. Staff - 20-39 years old. Patients - 70-89 years old. 60 subjects – 32 patients, 19 staff members, 8 patients' relatives, and 1 relative of a staff member.	**Outbreak description** Incubation period of secondary cases – median 48 hours (range 1-7 days). Attack rate – 25.4% for patients and 41.3% for staff. Infected healthcare staff who cared for patients at symptom initiation - 84%; 78% of them were in charge of changing bed linens and moving patients. The outbreak was controlled in 21 days. **Interventions** -Hand hygiene and unit cleaning/disinfection re-emphasized. -Staff excluded from work while ill. -Hand washing with antiseptic soap (chlorhexidine or povidone-iodine). Handwashing involved wetting hands, using liquid soap, scrubbing 15 seconds, rinsing with water, and drying hands with a disposable paper towel. -Rooms cleaned with 1% aldehyde or 0.1% chlorine-free bleach.	Cases were those who developed diarrhea (≥2 episodes/24 hours) and/or vomiting after detection of the first case. Secondary cases were relatives of cases who developed symptoms within 24 hours of visiting an ill family member on the ward. This outbreak met Kaplan criteria.	522_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
					16/32 stool samples were positive for norovirus genotype 2. Power and sample size not reported.	
Schmid, D; 2005 [175]	Descriptive study 1,2,3,4	To describe an outbreak of norovirus affecting an Austrian nursing home and a hospital	Patients and staff of a nursing home and a nearby hospital in Austria. 88% female among nursing home cases and 68% female among hospital cases. In the nursing home, median age of staff cases was 41 years and that of resident cases was 82 years. In the hospital, median age of staff cases was 37 years and that of patients was 81 years. 25 cases in the nursing home and 28 cases in the hospital	**Attack rates** *Nursing home* Residents – 18/23(73.9%) Staff – 7/18(38.9%) *Hospital* Patients – 10/46(21.7%) Staff – 18/60(30.0%) **Response to outbreak** *Nursing home* Hygiene measures were implemented without waiting for virological confirmation. Two more cases among the residents occurred during the first two days after the measures were implemented. *Hospital* After a total of 16 cases had occurred in 7 days, the hospital authorities instituted control measures after virological confirmation. After these were implemented two staff and two patients fell ill.	The two institutional clusters met the Kaplan criteria for a norovirus outbreak	388_RA
Weber, D; 2005 [176]	Descriptive study 1,3,4	To describe an outbreak of norovirus.	A locked pediatric psychiatric unit in North Carolina. Age of patients 6-12 years. Sample size not reported	**Outbreak description** The index patient was a non-compliant 9 year boy with autism and mood disorders who frequently soiled the environment with fecal material. 3 of 4 patients, 10 of 38 permanently assigned staff, 3 staff temporarily floating from other psychiatric units, and five family members developed gastroenteritis. Symptoms reported by 13 staff members included loose or watery stools in 92%, nausea in 85%, abdominal pain in 77%, vomiting in 69% and fever in 31% **Interventions** 1. The unit was closed to all admissions 2. All staff with symptoms of gastroenteritis were given sick leave 3. Ill staff were not allowed to work until asymptomatic for at least 2 days 4. Staff were precluded from eating and drinking in the unit 5. The entire unit was treated as an isolation room with all staff performing hand	Patients reported symptoms of gastroenteritis. norovirus was confirmed using RT-PCR in the index patient and 2 staff members.	405_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				hygiene and then donning gloves and a disposable gown 6. The unit was extensively cleaned and disinfected several times with 1:10 diluted hypochlorite (household bleach) 7. Hand hygiene with soap and water **Impact of interventions** (at 30 days after implementation) No subsequent cases of gastroenteritis were reported		
Lynn, S; 2004 [177]	Descriptive study 1,2,3,4	To describe outbreaks in two separate wards in a geriatric rehabilitation hospital and the role of infection control in limiting the spread.	Patients and staff in two wards in a geriatric rehabilitation hospital. 41 cases from the first outbreak. 24 cases from the second outbreak.	**First outbreak:** Attack rate – 57.1% for patients and 41% for staff. Outbreak duration – 14 days. Duration of ward closure – 11 days. Duration of staff sickness – mean, 1.2 days. Outcome – 1 patient died. **Second outbreak:** Attack rate – 56.5% for patients and 18% for staff. Outbreak duration – 16 days. Duration of ward closure – 6 days. Duration of staff sickness – mean, 3.5 days. **Interventions:** *Staffing guidelines* -Permanent staff worked in affected ward (wherever possible). -Staff needed to be symptom free for 48 hours before returning to work. -Staff without symptoms working in affected ward did not work anywhere else until 48 hours after completion of work in affected ward. -Casual staff who filled vacancies in affected ward remained there instead of also working on other wards. -Casual/bureau staff who had not worked in affected ward during the outbreak allocated to asymptomatic patients in non-infectious rooms. -All non-essential staff excluded when possible. *Precautions for any outbreak of vomiting and diarrhea* -Standard precautions at all times. -Hand hygiene stressed including when exiting ward. *Contact precautions* -Gloves and gown used when working in rooms with symptomatic patients. -Staff carried masks during acute outbreaks and used it if a patient had vomiting or diarrhea or to clean up vomit.	Cases were those with sudden onset of vomiting, with or without diarrhea. Other symptoms could include nausea, abdominal cramps, myalgia, headache, chills, and fever. The person had to have had contact with cases or in the environment/geographic area in which the outbreak was occurring. norovirus identified from stool sample using RT-PCR. Power and sample size not reported.	708_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Room placement -Contact precautions per room. -No patients transfers to other rooms. -If a patient was moved, another patient was not moved into the original bed space until the remainder of the room was symptom free for 48 to 72 hours. *Linen* -Linen carrier taken to bedside -Hot water soluble bags and infectious labels used for soiled linen bags. *Cleaning guidelines* -Contaminated surfaces, carpet, flooring, and equipment promptly cleaned and disinfected. -Shared patient equipment cleaned with diluted Chlorwhite between usage. -Labeled individual commodes. -Toilets cleaned after use (wherever possible) with dilute Chlorwhite. *Empty rooms* -Terminally cleaned using Chlorwhite. -Steam clean carpets at >150 pounds per square inch (psi). -Bedside curtain changed when patient vomited or had diarrhea. *Cleaning staff for general cleaning* -Protective clothing while working. -Diluted sodium hypochlorite used for all horizontal surfaces including bedrails, handrails, door handles. -Toilets cleaned three times a day. *Sodium hypochlorite (Chlorwhite)* -1000 ppm = 10 mls per 500 ml water in spray bottle. -Solution made daily. -Bottle and pump cleaned with detergent and water before refilling.		
Khanna, N; 2003 [178]	Descriptive study None	To describe an outbreak of norovirus gastroenteritis.	Patients and healthcare workers at a university hospital in Switzerland. Demographic details not provided. 63 cases	**Description of outbreak** There was no evidence for a water-borne, food-borne or environmental source. The source of the outbreak was most likely a patient admitted to the hospital. Once the outbreak was suspected, measures were instituted according to published guidelines, but the application of the guidelines proved difficult. **Interventions** Interventions from published guidelines (Chadwick, JHI 2000) that were found to be feasible were:	Patients suffered from clinical symptoms of acute gastroenteritis. norovirus was identified from fecal specimens by RT-PCR Study period from 28 February to 20 March	787_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				1. Cohorting nurses 2. Wearing gloves and gown 3. Cautioning visitors 4. Increasing the frequency of routine ward, bathroom and toilet cleaning Interventions from guidelines that were found to be difficult or not feasible were: 1. Isolating symptomatic patients 2. Washing hands with soap after patient contact 3. Excluding affected staff from the ward immediately and until 48 hrs symptom free (this resulted in severe staff shortage) 4. Closing ward and avoiding transfer (exceeded hospital resources and frequently multiple wards were affected at the same time) 5. Using hypochlorite to disinfect hard surfaces (it was thought that hypochlorite may result in incompatibilities with surface composition not resistant with bleach)	2001	
McCall, J; 2002 [179]	Descriptive study 1,2,3,4	To describe an outbreak of norovirus.	Staff and patients of an acute elderly ward in Ireland. Demographic characteristics not reported. 58 cases	**Interventions** 1. Where possible symptomatic individuals were nursed in isolation and when no single rooms were available, cohort-nursed 2. Disposable plastic gown and gloves for staff and visitors; careful hand hygiene 3. Ward closed to admissions 4. Non-essential personnel excluded from ward 5. Transfers of patients to other wards and areas of the hospital were avoided unless medically essential 6. Not discharged to nursing or residential accommodations; discharge to patient's own home permitted 7. Frequency of routine ward, bathroom and toilet cleaning increased to hourly 8. Staff instructed that vomit and feces spillages be cleaned and disinfected promptly 9. Hypochlorite used to disinfect hard surfaces after cleaning 10. Staff who covered wide areas of the hospital advised to visit unaffected wards before affected wards 11. Medical rotations were altered to avoid cross cover between affected and unaffected wards 12. Staff advised that if they became unwell they should go off duty immediately and should be free of vomiting and diarrhea for 48 hrs before returning to work 13. Affected wards were not re-opened until 72 hours after the last new case and 72 hours after uncontained vomiting and diarrhea 14. Affected wards were terminally cleaned at the end of the outbreak **Response to intervention** The control measures contained the spread of norovirus infection to one ward and stopped it in a few days	Case definition: A patient or staff member of the hospital who had acute onset of vomiting and/or diarrhea and who had a direct association with the elderly care ward without a negative sample. norovirus was confirmed using RT-PCR	890_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
Milazzo, A; 2002 [180]	Descriptive study 1,2,3,4	To describe an outbreak of norovirus gastroenteritis.	Residents and staff at an aged-care facility, 90/107 were females; 60% resided in the hostel, rest in the nursing home section. 107 residents, 75 staff	**Interventions** The interventions were based on published guidelines (Chadwick et al, JHI, 2000), specifically – staff were advised not to return to work for 48 hours after symptoms resolved.	A case was defined as a person living, working, visiting or epidemiologically linked to the aged-care facility with acute onset of diarrhea or vomiting between 14 August and 3 September 2000. Norovirus was confirmed with RT-PCR.	916_RA
Miller, M; 2002 [181]	Descriptive study 1,2,3,4	To describe an outbreak of norovirus gastroenteritis	Two aged care facilities and one hospital in Canberra., Australia Demographic characteristics not provided. 281 cases	**Description of outbreak** The outbreak lasted 32 days. Attack rates in the aged care facilities were 46.3%, 52.7% and that in the hospital was 55.2%. **Infection control challenges in the aged care facilities** 1. High pressure hoses in pan room 2. Lack of protective apparel in hose room 3. Lack of knowledge on body fluid spills 4. Limited access to spill kits 5. Lack of procedure for cleaning shower chairs 6. Inappropriate use of protective apparel when working with sick residents 7. Lack of adherence to staff sickness procedures 8. Transfers between institutions during outbreaks	Case definition: • at aged care facilities: a person who lived or worked at either institution and developed vomiting or diarrhea • at hospital: vomiting or diarrhea norovirus was detected using RT-PCR	879_RA
Hoyle, J; 2001 [182]	Descriptive study 1	To describe the challenges faced during an outbreak and its management.	Residents, staff and volunteers at a long term care facility in Australia. Demographic characteristics not reported. 76 residents; 25 staff and volunteers	**Interventions** 1. Education (especially about hand washing) 2. Collaborative development of an outbreak management guideline 3. Affected units were effectively quarantined until 14 days after the final case report in each unit. Quarantine strategies included: • Restricting symptomatic residents to the affected unit • Restricting staff and volunteer movements from affected to unaffected units • Restricting visitors to one unit per visit	A case was defined as any patient with diarrhea and/or vomiting within a 24 hour period. norovirus was confirmed to be the cause of the outbreak	3979_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				• Affected staff, visitors and volunteers were deemed to be infectious for 48 hours after cessation of symptoms and were excluded from the facility • Physiotherapy and occupational and divisional therapy activities were limited to essential services only. Staff in affected units had to remain there • Instigating cleaning regimens for all allied health equipment • Gaining the cooperation of nursing staff in actively encouraging volunteers and visitors to utilize the clinical hand washing facilities 4. Allocating one nurse to care for the affected residents after providing care to his/her unaffected residents 5. Environmental cleaning – 1% sodium hypochlorite to wipe down surfaces for spills of vomitus and feces, thorough facility wide clean, all continence pads treated as infectious waste, additional mop heads allocated to all the units **Management issues identified** 1. Lack of isolation/cohorting facilities 2. Movements of nursing staff, allied health staff and large numbers of volunteers 3. Staff shortages 4. Lack of clear outbreak management policies and procedures 5. Perception of the signs of an outbreak (e.g. vomiting and diarrhea) as a normal situation 6. Issues with cleaning protocols and practices **Positive outcomes** 1. Development of realistic gastroenteritis management guidelines 2. Development of an effective infection control relationship with staff 3. Development of a positive relationship with the public health unit 4. Development of a holistic approach to infection control surveillance, infection management and prevention Anecdotally, the key interventions were sick leave for staff, limiting the movements of both staff and patients, and early ward closure		
Cunney RJ, 2000[87]	Prospective controlled study 1,2,3,4	To investigate a hospital NLV outbreak.	Hospital outbreak N= 95 persons: 47 patients and 48 staff.	**Infection control practices** -Affected patients were cohorted -Admissions to and transfers from the geriatric ward were stopped -70% alcohol hand rub supplemented routine hand washing -Affected staff sent home until 48 hours after symptoms subsided -Decontamination procedures changed from standard phenolic solution to 2% hypochlorite solution	12 (13%) containing SRSV were solid phase immune electron microscopy (SPIEM) positive for NLV 25 (27%) sampes	1197_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				Food source Drinking water from the hospital water supply: 16 symptomatic and 6 nonsymptomatic (p=0.1)	contained small round featureless virus (SRFV) identified by direct EM and were negative on SPIEM Power and sample size not reported.	
Russo, PL; 1997 [183]	Descriptive study 1,2,3,4	To evaluate two outbreaks.	Patients and staff at an extended-care facility for the elderly and an acute care ward with an elderly population. Area 1 – 40 patients and 20 staff. Area 2 – 18 patients and 14 staff. Mean age – 79.1 years (range, 19-99).	**Attack rates** *First outbreak* Wards B and C – 50% Ward A – 33% *Second outbreak* Ward X – 49% **Interventions** *Admissions and discharges* -No patients admitted to or discharged from wards until outbreak ceased. -Patients discharged home if symptom free for 48 hours, with information and education, provided by the infection control department, given to patients' caregivers. *Visitors* -Visitors restricted to immediate family. Children discouraged from visiting until outbreak ceased. *New cases or patients requiring transfer* -Information sent to infection control on new cases or patients requiring transfer because of clinical deterioration. *Staff illness* -Affected staff remained off work until symptom free for 48 hours. *Nursing care* -Single use gowns and gloves worn when attending to patients with diarrhea and/or vomiting. Gowns were removed and disposed in a linen skip. Gloves thrown away and hands washed. *Handwashing* -Wash or disinfect hands after each patient contact. -Catering and cleaning staff instructed in hygiene and handwashing procedures by ward	Case was patient or staff with vomiting or ≥ 2 episodes of loose stools within a 24 hour period. Power and sample size not reported.	4006_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				nursing staff. *Restricting patient movements* -Patients should not attend other departments such as physiotherapy until the outbreak ceased. -Physiotherapy and occupational therapy limited to individual wards. *Staffing* -Staffing for each ward individualized. Staff should not be shared between wards. -Non-essential staff excluded until the outbreak ceased. *Environmental services staff* -Dedicated catering and cleaning staff required for the period of the outbreak. -Floors, locker, overbed tables, toilets, handwashing basins and taps, showers, surface areas in clean and dirty utility rooms cleaned with 100-200 ppm disinfectant containing sodium hypochlorite solution. -The infection control department determined when frequency of cleaning reduced. *Soiled linen* -Soiled linen placed in linen skip. Soiled linen should not be handled once in linen skip. Linen skips require frequent changing to prevent overfilling. Outcome: 2-3 weeks for the outbreaks declared over despite <24 hours for control measures to be implemented. Emphasized early notification and prompt staff furloughing **Costs (In outbreak 2 alone)** -Nursing staff sick leave - $7,600 -Bed closures - $10,600		
Stevenson, P; 1994 [184]	Descriptive study 1,2,3	To describe an outbreak in a hospital for the elderly.	Patients and staff at a UK hospital for the elderly. 95 patients and 69 staff (including 6 visitors) affected.	**Interventions** -Infected patients cohorted. -Special cleaning of toilet areas in affected wards. -Symptomatic staff excluded from work for 48 hours after symptom resolution. -Affected wards closed until 48 hour period with no new symptomatic patients or staff. -Patients needed 5 days of symptom resolution if being discharged to nursing home or elderly persons' home and 48 hours if returning to their own homes. **Enhanced Interventions** -Hospital closed 6 days after outbreak initiation until 4 days after the last case symptom free. -Cleaning regimen using hypochlorite solution (HAZ TABS) and alco-wipes. -Restricted staff cross-movement and patient communal gatherings.	Norwalk virus confirmed by EM. A case was a patient or staff with vomiting or diarrhea, with or without other symptoms, at the hospital on or after October 25, 1991. Six visitors were included as staff members.	1554_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				-Visiting restricted. -Discharges to nursing and residential homes stopped. -Guidelines and situation summary given to staff with daily updated press statements. -Wards symptom free for 4 days given a final deep clean with 2% hypochlorite solution (including carpets, curtains, walls, and other equipment) prior to reopening. -Reopening prohibited if any staff or patient had diarrhea or vomiting. If only diarrhea, assessment by duty medical officer done to establish if the patient was suffering from viral gastroenteritis.	Power and sample size not reported.	
Hudson, JB; 2007 [185]	Basic science	To evaluate the efficacy of ozone gas from a generator (Viroforce) in inactivating norovirus and its surrogate FCV in dried samples in an office, hotel room, and cruise liner cabin.	Virus samples (50-100uL) were dried in duplicate on surfaces including sterile plastic. Ozone level was maintained at 20-25 ppm for 20 minutes, the rapid humidifying device (RHD) was activated for a 5 minute burst of water vapor, both the generator and RHD were switched off for 10 minutes to allow for incubation in the humid atmosphere, and the scrubber was then turned on to remove all ozone gas. When ozone levels decreased to less than 1 ppm, the door was opened and test samples retrieved for testing.	**Results from field test in office following standard ozone protocol** *All results: Fraction of control in Pfu (Log_{10}); Fraction of control in RT-PCR (Log_{10})* FCV :0.012 (-1.92); 0.029 (-1.54) FCV + FBS: 0.017 (-1.77); 0.021 (-1.68) FCV + stool: 0.015 (-1.82); 0.020 (-1.70) *All results: Fraction of control in RT-PCR (Log_{10})* norovirus sample 1: 0.070 (-1.15) norovirus sample 2: 0.055 (-1.26) norovirus sample 3: 0.046 (-1.34) **Results from field test in hotel room following standard ozone protocol** *All results: Fraction of control in Pfu (Log_{10}) ; Fraction of control in RT-PCR (Log_{10})* FCV, bathroom: 0 (<-4.0); 0.077 (-1.11) FCV, bed: <0.0002 (<-3.7); 0.077 (-1.11) FCV, table: 0 (<-4.0); 0.075 (-1.12) **Results from cruise liner cabin following standard ozone protocol** Treated (bathroom, bed, and table): $<10^1$ Pfu/mL; Surviving fraction <0.0002; RT-PCR surviving fraction 0.003-0.03 **Results on different surfaces following standard ozone protocol** *All results – fraction of control* Plastic – FCV infectivity ≤6 x 10^{-5}; FCV QRT-PCR 0.0013-0.0016; norovirus QRT-PCR 0.05-0.069 Fabric – FCV infectivity ≤3 x 10^{-4}; FCV QRT-PCR 0.0036-0.0048; norovirus QRT-PCR 0.056-0.065 Cotton – FCV infectivity ≤3 x 10^{-5}; FCV QRT-PCR 0.076-0.079; norovirus QRT-PCR 0.030-0.031 Carpet – FCV infectivity ≤4 x 10^{-5}; FCV QRT-PCR 0.0028-0.0032; norovirus QRT-PCR 0.042-0.059 Virus-containing samples dried onto hard and soft surfaces were equally vulnerable to	Norovirus measured by RT-PCR and FCV by QRT-PCR and virus infectivity assays. Feline bovine serum (FBS) Pfu = plaque forming units/mL **Control values** *Field test in office* *FCV infectivity* 5.1 x 10^4 Pfu/mL 116-218 ng RNA by PCR *norovirus infectivity* norovirus sample 1 = 58.15 ng RNA norovirus sample 2 = 129.5 ng RNA norovirus sample 3 = 114.1 ng RNA *Field test in hotel room* *FCV infectivity* 8.0 x 10^4 Pfu/mL 415.5 ng RNA by PCR *Field test in cruise liner cabin* *FCV infectivity*	122_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				ozone. Some potential toxicity issues, especially in areas with high traffic	5.37 x 10^4 Pfu/mL *Field test for different surfaces* *FCV infectivity* 2.7-3.6 x 105 Pfu *FCV QRT-PCR* 18.7-57.3 ng RNA *norovirus QRT-PCR* 98.6-132.7 ng RNA	
Park GW, 2007 [186]	Basic Science	To evaluate the efficacy of sterilox hypochlorous acid (HOCl) solution (HAS) to reduce norovirus both in aqueous suspensions and on inanimate carriers. HOCl was further tested as a fog to decontaminate large spaces	No. 4 finish-polished stainless steel and ceramic tiles were used as representative nonporous andporous surfaces.	Exposing virus-contaminated carriers of ceramic tile (porous) and stainless steel (nonporous) to 20 to 200 ppm of HOCl solution resulted in ≥ 99.9% (≥ 3 $\log_{10}$) reductions of both infectivity and RNA titers of tested viruses within 10 min of exposure time. HOCl fogged in a confined space reduced the infectivity and RNA titers of norovirus, MNV, and MS2 on these carriers by at least 99.9% (3 $\log_{10}$) regardless of carrier location and orientation.	HOCl effectiveness was evaluated using nonculturable human norovirus measured by RT-PCR and two surrogate viruses, coliphage MS2 and MNV.	89_IL
Poschetto, LF; 2007 [187]	Basic science	To evaluate the efficacy of an organic acid (Venno Vet 1 Super), an aldehyde (Venno FF Super), a halogen compound (sodium hypochlorite solution), and	Known amounts of virus suspensions were incubated with disinfectants. Viral RNA levels were checked pre- and post-disinfection.	**Virucidal efficacies of disinfectants** *All results – minutes (titer in $\log_{10}$ RTPCRU/ml)* Organic acid (3%) FCV – 15 (5); 30 (5); 60 (5); 120 (5) norovirus – 15 (5); 30 (5); 60 (5); 120 (5) Organic acid (4%) FCV – 15 (3); 30 (2); 60 (2); 120 (2) norovirus – 15 (4); 30 (4); 60 (4); 120 (4) Organic acid (5%) norovirus – 15 (4); 30 (3); 60 (2); 120 (2) Aldehyde (0.1%) FCV – 15 (5); 30 (4); 60 (5); 120 (5) norovirus – 15 (5); 30 (5); 60 (5); 120 (5)	The criterion normally set for virucidal efficacy is 99.9% (3 $\log_{10}$) – these results are highlighted.	067_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
		peroxide (Oxystrong FG) in inactivating norovirus and FCV.		Aldehyde (0.5%) FCV – 15 (4); 30 (4); 60 (3); 120 (3) norovirus – 15 (5); 30 (5); 60 (5); 120 (5) Aldehyde (1%) norovirus – 15 (4); 30 (4); 60 (4); 120 (4) Aldehyde (2%) norovirus – 15 (4); 30 (4); 60 (3); 120 (3) Halogen compound (1%) FCV – 15 (5); 30 (5); 60 (5); 120 (5) norovirus – 15 (4); 30 (3); 60 (3); 120 (4) Halogen compound (6,000 ppm free chlorine) FCV – 15 (2); 30 (2); 60 (2); 120 (2) norovirus – 15 (≤1); 30 (2); 60 (≤1); 120 (2) Halogen compound (1.2%) FCV – 15 (5); 30 (4); 60 (5); 120 (5) norovirus – 15 (4); 30 (4); 60 (4); 120 (4) Halogen compound (7,000 ppm free chlorine) FCV – 15 (2); 30 (2); 60 (≤1); 120 (2) norovirus – 15 (≤1); 30 (≤1); 60 (≤1); 120 (≤1) Peroxide (1%) FCV – 15 (2); 30 (3); 60 (2); 120 (2) norovirus – 15 (3); 30 (3); 60 (2); 120 (2) Peroxide (2%) FCV – 15 (2); 30 (2); 60 (2); 120 (2) norovirus – 15 (3); 30 (3); 60 (2); 120 (2) **Disinfectant concentrations and contact times associated with the greatest FCV and norovirus titer reduction** *All results Disinfectant [reduction factor (RF) in log10] – Conditions for FCV and norovirus* Organic acid (3) – FCV 4%, 30 minutes; norovirus 5%, 60 minutes Aldehyde (2) – FCV 0.5%, 60 minutes; norovirus 2%, 60-120 minutes Halogen compound (≥3) – FCV 1% (6,000 ppm free chlorine), 15 minutes; norovirus 1% (6,000 ppm free chlorine), 15 minutes Peroxide (3) – FCV 1%, 60 minutes or 2%, 15 minutes; norovirus 1%, 60 minutes or 2%, 60 minutes **Conclusions** All disinfectants, except the aldehyde, were effective on FCV. According to RT-PCR results, 5% organic acid, 1% peroxide, not less than 2% aldehyde with a contact time of 1 h, and a 1% halogen compound with 6,000 ppm of free chlorine and a contact time of 15 minutes, are required for safe disinfection.		

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
Jimenez, L; 2006 [188]	Basic science study N/A	To determine the virucidal effectiveness of R-82, a quarternary ammonium compound disinfectant. This was prepared as 1:256 dilutions in water with a hardness of 400 ppm calcium carbonate for 10 minutes. Hypochlorite concentrations of 100 ± 10 and 1000 ± 10 ppm were also analyzed as controls.	Feline calcivirus (FCV) suspensions. Study was conducted in New Jersey, US. N/A	**Reductions in FCV in log_{10} MPN/mL at 10 min contact time** *Initial testing* R-82 – 6.6 (complete inactivation) Hypochlorite 100 ± 10 ppm – 3.2 Hypochlorite 1000 ± 10 ppm – 6.6 (complete inactivation) *Confirmatory testing* R-82 – 6.4 (complete inactivation) Hypochlorite 100 ± 10 ppm – 2.8 Hypochlorite 1000 ± 10 ppm – 6.4 (complete inactivation)	The reduction of infectious virus (defined as FCV with cytopathic effects) were expressed as log_{10} most probable number (MPN)/mL. The log_{10} reduction for FCV was calculated as the difference between the disinfectant and plate recovery control.	3879_RA
Kramer, A; 2006 [189]	Basic science	To test the virucidal activity (reduction in viral titer) of a new hand disinfectant with reduced ethanol content (55%) in combination with 10% propan-1-ol, 5.9% propan-1.2-diol, 5.7% butan-1.3-diol and 0.7%	FCV strain F9 both in vitro and in vivo (fingerpad tests using human volunteers – 3 male, 4 female). 7	**Dilution of test product demonstrating virucidal efficacy (RF≥4) against FCV** 80% dilution for a contact time of 0.5 min **Reduction of FCV titers** *All results mean log10 RF; P value for comparison with test product* Test product vs. 70% ethanol – 2.38 vs. 0.68; P<0.01 Test product vs. 70% propan-1-ol – 2.38 vs. 0.74; P<0.01 Test product vs. standard hard water – 2.38 vs. 1.39; P<0.01	Virucidal efficacy was measured as log_{10} reduction in viral titers – called reduction factor (RF). A disinfectant solution was considered to have virucidal efficacy if, within the tested exposure period, the titre was reduced at least 10^4 fold (RF≥4)	374_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
		phosphoric acid. For in vivo tests, the test product was compared with 70% ethanol, 70% propan-1-ol and standard hard water.				
Malik, Y; 2006 [190]	Basic science study N/A	To evaluate five disinfectants against FCV on various carpets and fabrics to detect percentage inactivation of virus. The five disinfectants tested were: 1. Metricide – activated 2.6% glutaraldehyde (undiluted) 2. Microbac-II – 4.75% o-benzyl p-chlorophenol and 4.75% o-phenylphenol (1:128 dilution) 3. 10% sodium bicarbonate and 10% quarternary	*Fabrics* 1. 100% cotton 2. 100% polyester 3. Cotton blend (35:65 blend of cotton and polyester) *Carpets* 1. Olefin 2. Polyester 3. Nylon 4. Blended carpet (85:15 blend of nylon and olefin) N/A	All results are percentage inactivation of FCV at 1, 5 and 10 min **Fabrics** *1. 100% cotton* Metricide – 99.99; 99.99; 100.00 Microbac-II – 85.63; 73.40; 98.72 Sodium bicarbonate and quarternary ammonium compound – 86.20; 90.00; 97.34 GermEX – 98.26; 99.55; 99.86 Sodium bicarbonate and glutaraldehyde – 95.63; 99.12; 99.55 *2. 100% polyester* Metricide – 99.99; 99.99; 100.00 Microbac-II – 71.73; 98.32; 99.00 Sodium bicarbonate and quarternary ammonium compound – 94.56; 90.00; 92.40 GermEX – 82.17; 69.60; 91.60 Sodium bicarbonate and glutaraldehyde – 73.91; 83.52; 96.96 *3. Cotton blend* Metricide – 99.99; 99.99; 100.00 Microbac-II – 77.61; 86.20; 95.21 Sodium bicarbonate and quarternary ammonium compound – 99.00; 98.04; 95.43 GermEX – 99.00; 98.04; 96.30 Sodium bicarbonate and glutaraldehyde – 99.38; 99.25; 97.39 **Carpets** *1. Olefin* Metricide – 99.91; 99.97; 99.95 Microbac-II – 77.61; 84.25; 73.84 Sodium bicarbonate and quarternary ammonium compound – 0; 62.0; 83.83 GermEX – 60.95; 92.10; 97.00 Sodium bicarbonate and glutaraldehyde – 78.09; 88.00; 96.76	% virus inactivation = 100 – (amount of virus from disinfectant-treated pieces/amount of virus from negative-control pieces) × 100. Average of 3 experiments was used. Virus was grown in feline kidney cells.	313_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
		ammonium compound (1:32 dilution) 4. GermEX – 70% isopropanol (undiluted) 5. 2.5% sodium bicarbonate and 1.3% glutaraldehyde (1:32 dilution)		*2. Polyester* Metricide – 94.54; 100.00; 100.00 Microbac-II – 88.63; 88.29; 96.91 Sodium bicarbonate and quarternary ammonium compound – 82.72; 77.65; 95.53 GermEX – 88.63; 91.70; 78.72 Sodium bicarbonate and glutaraldehyde – 97.90; 95.10; 98.14 *3. Nylon* Metricide – 99.93; 99.95; 100.00 Microbac-II – 38.18; 36.95; 60.26 Sodium bicarbonate and quarternary ammonium compound – 0; 17.31; 17.21 GermEX – 52.72; 93.69; 91.72 Sodium bicarbonate and glutaraldehyde –67.27; 71.73; 90.00 *4. Blended carpet* Metricide – 80.00; 97.80; 99.68 Microbac-II – 55.17; 38.00; 68.39 Sodium bicarbonate and quarternary ammonium compound – 80.00; 38.00; 45.90 GermEX – 80.00; 73.80; 68.39 Sodium bicarbonate and glutaraldehyde – 97.58; 91.90; 90.00		
Malik, Y; 2006 [191]	Basic science study N/A	To compare the virucidal activity of ethanol and isopropyl alcohol against dried feline calcivirus (FCV). Control was exposure to phosphate buffered saline (PBS).	F-9 strain of FCV. Study was conducted in US. N/A	**Percent virus reduction** *All results are reductions at a contact time of 1,3 and 10 minutes respectively at each concentration of the disinfectant in %* *Ethyl alcohol* 10 – 86.49; 91.16; 95.00 20 – 88.37; 88.37; 86.49 30 – 88.37; 81.65; 88.37 40 – 93.70; 99.19; 84.10 50 – 98.28; 97.55; 90.20 60 – 98.11; 98.65; 90.20 70 – 99.19; 98.41; 94.50 80 – 98.43; 98.50; 94.50 90 – 99.35; 97.49; 99.49 100 – 98.46; 97.65; 98.06 **Isopropyl alcohol** 10 – 95.07; 87.81; 87.81 20 – 80.29; 91.64; 80.83 30 – 90.46; 90.00; 83.13 40 – 99.30; 94.44; 94.75	% virus reduction was calculated as [($V_{control}$ – $V_{treated}$)/ $V_{control}$] X 100	3891_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				50 – 99.59; 99.52; 99.12 60 – 99.84; 99.76; 99.79 70 – 97.57; 98.94; 99.47 80 – 97.37; 99.12; 99.46 90 – 97.37; 98.14; 99.57 100 – 97.36; 96.59; 96.65 Summary: Ethanol at 70% and 90% concentrations was most effective at killing FCV within 1 minute; isopropanol effective at 50% and 70% but none of the alcohols able to achieve 3 log reduction in FCV (>99.9% kill).		
Malik, Y; 2006 [192]	Basic science study N/A	To evaluate the efficacy of the following compounds against FCV dried on a stainless steel surface: 1. Sodium Bicarbonate 1% + 1.3% glutaraldehyde 2. Sodium Bicarbonate 2.5% + 1.3% glutaraldehyde 3. Sodium Bicarbonate 1.0% + activated dialdehyde 4. Sodium Bicarbonate 2.5% + activated dialdehyde 5. Sodium Bicarbonate 2.0% + 2.0%	F-9 strain of FCV. Study was conducted in US. N/A	**Percent virus reduction** *All results are reductions at a contact time of 1,3 and 10 minutes respectively at each concentration of sodium bicarbonate in %* 1 – 97.22; 97.22; 98.60 2 – 97.22; 98.14; 99.60 5 – 99.22; 99.40; 99.81 10 – 99.99; 99.99; ≥99.99 20 - 99.99; ≥99.99; ≥99.99 *All results are reductions at a contact time of 1,3 and 10 minutes respectively for each disinfectant* Sodium Bicarbonate 1% + 1.3% glutaraldehyde – 99.99; 99.99; 99.99 Sodium Bicarbonate 2.5% + 1.3% glutaraldehyde – 99.99; 99.99; 99.99 Sodium Bicarbonate 1.0% + activated dialdehyde – 99.00; 99.00; 99.99 Sodium Bicarbonate 2.5% + activated dialdehyde – 99.99; 99.99; 99.99 Sodium Bicarbonate 2.0% + 2.0% hydrogen peroxide – 99.00; 99.00; 99.68	% reduction = 100 – (virus counts eluted after test product treatment/virus counts eluted from control well disks) x 100	4234_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
		hydrogen peroxide				
Kampf, G; 2005 [193]	Basic science	To investigate the efficacy of 3 ethanol-based hand rubs against FCV on artificially contaminated hands.	German volunteers had their fingers contaminated with virus suspension with or without organic load and decontaminated with one of the 3 ethanol-based handrubs compared to 70% N-propanol or 70% ethanol to determine their efficacy against FCV. 4 volunteers.	**Reduction in FCV infectivity** *Mean log_{10} reduction factor hand rub (n=16), 70% ethanol (n=8): p value* Reference alcohols – N/A, 1.45; N/A Sterillium Virugaard – 2.17, 1.56; 0.17 Sterillium Rub – 1.25, 1.03; 0.20 Desderman N – 1.07, 1.27; 0.47 *Mean log_{10} reduction factor of hand rub (n=16), 70% propan-1-oll (n=8); p value* Reference alcohols – N/A, 0.95; N/A Sterillium Virugaard – 1.63, 0.95; 0.0003 Sterillium Rub – 1.43, 1.09; 0.03 Desderman N – 0.78, 0.97; 0.35 Summary: Ethanol superior to isopropan-1-ol	Cases received Sterillium Virugard, 95% ethanol, Sterillium Rub, 80% ethanol, or Deserman N, 75.1% ethanol. Controls received N-propanol (70%, w/w) and ethanol (70%, w/w), which have previously been described to be virucidal against FCV.	510_IL
Barker, J; 2004 [194]	Basic science	To study the transfer of norovirus from contaminated fecal material via fingers and cloths to other surfaces using RT-PCR and to assess the effectiveness of detergent and disinfectant based cleaning regimens.	A homogenized clinical fecal sample positive for norovirus genogroup II was used. A fecal sample negative for norovirus was used as a negative control. **Transfer of norovirus by fingers to surfaces** *Primary transfer* Fecal sample diluted in phosphate buffered saline was absorbed on toilet paper in a Petri dish. The experimenter's fingertips were pressed on to the contaminated tissue for 10 seconds, and dried for 15 seconds at room temperature.	**Transfer of norovirus by fingers to surfaces** *Primary Transfer* 4 experiments using 8 clean melamine surfaces: 4 surfaces – all 4 experiments norovirus positive 2 surfaces – 3/4 experiments positive 1 surface – 1/4 experiments positive 1 surface – 0/4 experiments positive *Secondary Transfer* norovirus transferred from primary surface to 4/10 door handles, 5/10 telephone receivers, and 3/10 taps. **Cleaning and disinfection studies** Methods 1, 2 and 3 failed to eliminate norovirus in 14 experiments even when the cloth was re-soaked and the melamine surface rewiped. If the cloth was used to wipe a second clean surface, norovirus was recovered from that surface and from the fingers of study participants. Methods 4 and 5 eliminated norovirus from the surface in a portion of cases. When the surface tested negative, second surfaces and fingers also tested negative. norovirus could still be detected in 28% of surfaces at 5 minute and 21% after 1 minute. In cases where norovirus remained, there was 100% transfer to a second clean surface and 75% transfer to fingers. Method 6 completely eliminated norovirus.	Hypochlorite disinfectant/cleaner (HDC) containing 5000 ppm of available chlorine and 4% (w/v) of an anionic surfactant (supplied by Lever Brothers, Port Sunlight, UK).	628_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			Contaminated fingers were then pressed on clean melamine surfaces for 10 seconds and left at room temperature for 15 minutes before testing for norovirus. *Secondary transfer* After allowing contaminated melamine surface to dry at room temperature for 15 minutes, clean dry fingers touched the surfaces and then touched a telephone receiver, a tap handle, and a door handle. Secondary surfaces were left at room temperature for 15 minutes before testing for norovirus. **Cleaning and disinfection studies** 6 melamine surfaces were contaminated with 10µL fecal sample and dried at room temperature for 15 minutes. They underwent the following protocols and were sampled for norovirus after cleaning: 1) Untreated control 2) Cleaning with cloth			

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			soaked in detergent solution for 10 seconds 3) Cleaning with used cloth initially soaked in detergent solution for 10 seconds, then later rinsed in detergent solution after use, and then used to rewipe the surface for 10 seconds. 4) Hypochlorite disinfectant/cleaner (HDC) applied to surface for 1 minute followed by wiping of surface with cloth soaked in detergent solution for 10 seconds. 5) Similar to 4, except HDC applied for 5 minutes. 6) Gross fecal matter removed from the surface by wiping with a cloth soaked in detergent solution for 10 seconds, followed by surface disinfection with HDC for 1 minute, followed by wiping of surface with cloth soaked in detergent solution for 10 seconds.			
Duizer E, 2004 [195]	Basic Science	To investigate the inactivation of the enteric canine CaCV no. 48 and the	N/A	**Thermal inactivation** Inactivation of CaCV and FCV: 4C: <1D inactivation in 2 weeks 20C: 3D inactivation 1 week Between 37 - 56C: 3D inactivation decreased from 24 hours to 8 minutes Heating to 71.3C: 3D inactivation in 1 minute	D = 1 $\log_{10}$, calculated by dividing the $TCID_{50}$ of the treated sample by the $TCID_{50}$ of the untreated sample	643_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
		respiratory FCV F9.		Reduction of infectivity by five cycles of freezing and thawing was 0.44 ± 012 D for CaCV and 0.34 ± 0.18D for FCV **UV inactivation** 21 mJ/cm^2 for CaCV and 22mJ/cm^2 for FeCV: 2D inactivation 34 mJ/cm^2 for CaCV and FeCV: 3D inactivation **pH stability** pH<= 5 and pH>=10: >5D inactivation for CaCV pH 9: 4D reduction for FeCV and 3D reduction for CaCV pH 6: 2D reduction for FeCV and 4D reduction for CaCV pH<=2 and pH>=10: >5D inactivation for FCV **Inactivation by 70% ethanol** Inactivation of CaCV and FCV: <2D reduction in $TCID_{50}$ after 8 minutes 3D reduction after 30 minutes **Inactivation by sodium hypochlorite** Up to 30 ppm free chlorine: <1D inactivation 300 ppm: >3D inactivation for CaCV and <2D inactivation for FCV 3,000 ppm: complete inactivation (>5D) of FeCV and CaCV in 10 and 30 minutes at room temperature		
Gehrke, C; 2003 [196]	Basic science	To evaluate the efficacy of 3 types of alcohol against FCV as a surrogate for norovirus on fingertips.	**In vitro inactivation experiments** One part virus suspension mixed with one part double distilled water and eight parts alcohol in different concentrations to determine efficacy of alcohol products. **In vivo inactivation experiments** Fingertips of volunteers from Germany were artificially contaminated	**In vitro inactivation experiments** *All results Alcohol with concentration – Reduction in titer in log_{10} ID_{50} after different time periods; Time to ≥ 4 log_{10} reduction in titer* Ethanol 50% - 2.19 at 0.5 min, 3.65 at 1.0 min, ≥4.44 at 3.0 min, ≥4.50 at 5.0 min; 3.0 min Ethanol 70% - 3.55, ≥3.83, ≥5.00, ≥5.19; 3.0 min Ethanol 80% - 2.19, 2.97, 3.88, ≥4.25; 5.0 min 1-Propanol 50% - ≥4.13, ≥4.31, ≥5.13, ≥4.73; 0.5 min 1-Propanol 70% - ≥4.06, ≥4.06, ≥4.13, ≥4.13; 0.5 min 1-Propanol 80% - 1.90, ≥3.58, ≥4.13, ≥3.98; 3.0 min 2-Propanol 50% - 2.31, 3.22, ≥4.90, ≥5.47; 3.0 min 2-Propanol 70% - 2.35, 2.90, ≥3.92, ≥4.22; 5.0 min 2-Propanol 80% - 1.35, 1.27, 1.88, 2.38; >5.0 min *Extrapolated data*		730_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			with FCV to determine the efficacy of virus elimination using different alcohol products. The tested alcohol products included ethanol, and 1- and 2-propanol.	The following concentrations had the greatest virus-inactivating properties: Ethanol 67% after 1 min with a log_{10} reduction factor of 3.8. 2-Propanol 58% after 1 min with a log_{10} reduction factor of 4.9. 1-Propanol 60% after 30 sec with a log_{10} reduction factor of 4.3. **In vivo inactivation experiments** *All results Alcohol (concentration; exposure time; No. fingertips) – Reduction of FCV titer in log_{10} ID_{50} ± SD* Ethanol (70%; 30 sec; 16) – 3.78 ± 0.83 Ethanol (90%; 30 sec; 8) – 2.84 ± 0.64 1-Propanol (70%; 30 sec; 16) – 3.58 ± 0.92 1-Propanol (90%; 30 sec; 8) – 1.38 ± 0.33 2-Propanol (70%; 30 sec; 16) – 2.15 ± 0.50 2-Propanol (90%; 30 sec; 8) – 0.76 ± 0.19 Hard water (N/A; 30 sec; 36) – 1.23 ± 0.44 **Conclusions** In vitro experiments showed that 1-propanol was most effective The greatest efficacy did not occur at the highest concentrations (80%). In contrast to the in vitro studies, in vivo 70% ethanol showed the greatest efficacy.		
Lin, C; 2003 [197]	Basic science	To evaluate different hand washing agents against natural and artificial fingernails contaminated with Ecoli and CaCV.	Volunteers from Georgia with artificial and natural nails were artificially contaminated with ground beef containing E coli JM109 or artificial feces containing FCV to evaluate the efficacy of the following agents: handwashing with tap water, regular liquid soap (Ivory, Proctor and Gamble), antibacterial liquid soap, (Dial Gol, active ingredient triclosan) alcohol-based hand sanitizer gel (Purell, 62% ethanol), regular liquid soap followed by	**FCV** *All six handwashing procedures combined - Before vs after handwashing FCV in -log $TCID_{50}$ ± SD* Natural nail – 3.06 ± 0.47 vs 1.15 ± 0.75 Artificial nail – 3.69 ± 0.52 vs 2.18 ± 0.98 *All results for Handwashing agents – reductions in counts in - log $TCID_{50}$ ± SD* *Tap water* Natural nail – 1.97 ± 0.68 Artificial nail – 1.22 ± 0.86 *Soap* Natural nail – 1.82 ± 0.46 Artificial nail – 1.89 ± 0.31 *Antibacterial soap* Natural nail – 2.26 ± 0.42 Artificial nail – 1.65 ± 0.19 *Hand sanitizer* Natural nail – 0.86 ± 0.55	Highlighted p≤0.05	769_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
			alcohol gel, and regular liquid soap plus a nailbrush. Average age – 45 5 with artificial nails – all female 5 with natural nails – 3 female and 2 male	Artificial nail – 0.43 ± 0.47 *Soap plus sanitizer* Natural nail – 2.13 ± 0.93 Artificial nail – 1.85 ± 0.69 *Soap plus nailbrush* Natural nail – 2.54 ± 0.57 Artificial nail – 0.41 ± 0.79 **Combined data** Lower non-statistical reductions of Ecoli and FCV counts obtained for artificial vs natural fingernails (p>0.05). Significantly higher Ecoli and FCV counts were recovered from hands with artificial vs natural nails before and after hand washing (p<=0.05). Microbial cell numbers were correlated with fingernail length, with greater numbers for those with longer nails (p>0.05). **Conclusions** Best practices for fingernail sanitation of food handlers may be to keep fingernails short , natural, and scrub with soap and nailbrush when washing hands.		
Nuanualsuwan,S ; 2002 [198]	Basic science study N/A	To evaluate ultraviolet (UV) inactivation of feline calcivirus (FCV) and to compare it to hepatitis A virus, poliovirus type 1 and two small, round coliphages (MS2 and φX174).	FCV and other viruses (hepatitis A virus, poliovirus type 1 and two small, round coliphages - MS2 and φX174). N	**Dose in mW s/cm² required to reduce viral titer by 1 log_{10}** FCV – 47.85 Hepatitis A Virus – 36.50 Poliovirus type 1 – 24.10 MS2 – 23.04 φX174 – 15.48 The UV inactivation curve of FCV was not statistically different from Hepatitis A virus (P>0.05), but was significantly different from Poliovirus type 1, MS2 and φX174 (P<0.05)		4603_RA
Gulati, BR; 2001 [199]	Basic science	To use FCV as a surrogate to determine the potential	The following products were tested for their efficacy against FCV on artificially	**1 minute contact time** **-Not effective in any of the tests and no further details given** **10 minute contact time**	An agent was considered effective if the virus titer decreased at least 3	5985_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
		efficacy of disinfectants against norovirus on fresh fruit and produce, and food-contact surfaces.	contaminated: *Stainless steel food contact surfaces* – 5.25% sodium hypochlorite (Fox-chlor, Jane Fox, Minn); 1.75% iodine and 6.5% phosphoric acid (Mikroklene, Ecolab, St. Paul, Minn); three quarternary ammonium compouns (QACs) (Microquat and Oasis 144, Ecolab and UMQ, Chemical Specialties Lab, Fairmont, Minn); 15% peroxyacetic acid and 11% hydrogen peroxide (Victory, Ecolab); and two phenolic products (Lysol IC, Reckitt an Colman, Montvale, NJ, and Microbac II, Ecolab) *Strawberry and lettuce* - 5.25% sodium hypochlorite (Fox-chlor), QAC (Oasis 144), and 15% peroxyacetic acid and 11% hydrogen peroxide (Victory). Products tested at one, two, or four times manufacturers' recommended concentrations for contact times of 1 and 10 minutes.	***Food contact surfaces*** *All results – Log_{10} FCV reduction ± SD* 9% QAC 1:200 (450 ppm) – 0.3 ± 0.05 9% QAC 1:100 (900 ppm) – 0.0 ± 0.0 9% QAC 1:50 (1800 ppm) – 2.3 ± 0.05 10% QAC 1:256 (400 ppm) – 0.7 ± 0.1 10% QAC 1:128 (800 ppm) – 1.0 ± 0.1 10% QAC 1:64 (1600 ppm) – 2.0 ± 0.05 5% QAC and 2% sodium bicarbonate 1:64 (780 ppm of QAC) – 0.4 ± 0.05 5% QAC and 2% sodium bicarbonate 1:32 (1560 ppm of QAC) – 3.3 ± 0.1 5% QAC and 2% sodium bicarbonate 1:16 (3120 ppm of QAC) – 3.4 ± 0.05 5.25% sodium hypochlorite (200 ppm of free chlorine) – 0.3 ± 0.05 5.25% sodium hypochlorite (400 ppm of free chlorine) – 0.3 ± 0.0 5.25% sodium hypochlorite (800 ppm of free chlorine) – 1.1 ± 0.05 15% peroxyacetic acid and 11% hydrogen peroxide 1:2000 – 0.4 ± 0.1 15% peroxyacetic acid and 11% hydrogen peroxide 1:1000 – 0.6 ± 0.05 15% peroxyacetic acid and 11% hydrogen peroxide 1:500 – 3.0 ± 0.0 1.75% iodine and 6.5% phosphoric acid (75 ppm of titratable iodine) – 0.0 ± 0.0 1.75% iodine and 6.5% phosphoric acid (150 ppm of titratable iodine) – 0.0 ± 0.0 1.75% iodine and 6.5% phosphoric acid (300 ppm of titratable iodine) – 2.0 ± 0.1 4.75% o-benzyl p-chlorophenol and 4.75% o-phenylphenol 1:256 – 1.5 ± 0.05 4.75% o-benzyl p-chlorophenol and 4.75% o-phenylphenol 1:128 – 6.2 ± 0.2 4.75% o-benzyl p-chlorophenol and 4.75% o-phenylphenol 1:64 – 7.0 ± 0.2 5% o-benzyl p-chlorophenol and 10.5% o-phenylphenol 1:200 – 0.4 ± 0.1 5% o-benzyl p-chlorophenol and 10.5% o-phenylphenol 1:100 – 0.4 ± 0.1 5% o-benzyl p-chlorophenol and 10.5% o-phenylphenol 1:50 – 5.6 ± 0.2 ***Fresh produce*** *All results – Log_{10} FCV reduction ± SD* 15% peroxyacetic acid and 11% hydrogen peroxide 1:2000 – Strawberry 0 ± 0.00; Lettuce 0 ± 0.00 15% peroxyacetic acid and 11% hydrogen peroxide 1:1000 – Strawberry 1.0 ± 0.1; Lettuce 2.0 ± 0.1 15% peroxyacetic acid and 11% hydrogen peroxide 1:500 – Strawberry 3.0 ± 0.06; Lettuce 3.0 ± 0.06	log_{10} (99.9%) compared to untreated controls – significant results highlighted. Disinfectants and sanitizers diluted in sterile tap water immediately before use.	

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
				5.25% sodium hypochlorite (200 ppm of free chlorine) – Strawberry 0 ± 0.0; Lettuce 0 ± 0.0 5.25% sodium hypochlorite (400 ppm of free chlorine) – Strawberry 0 ± 0.0; Lettuce 0 ± 0.0 5.25% sodium hypochlorite (800 ppm of free chlorine) – Strawberry 1.0 ± 0.06; Lettuce 1.5 ± 0.05 10% n-alkyl (50% C14, 40% C12, 10% C16) imethyl benzyl ammonium chloride 1:512 (200 ppm) – Strawberry 0 ± 0.0; Lettuce 0 ± 0.0 10% n-alkyl (50% C14, 40% C12, 10% C16) imethyl benzyl ammonium chloride 1:256 (400 ppm) – Strawberry 0 ± 0.0; Lettuce 0 ± 0.0 10% n-alkyl (50% C14, 40% C12, 10% C16) imethyl benzyl ammonium chloride 1:128 (800 ppm) – Strawberry 1.5 ± 0.1; Lettuce 2.0 ± 0.1 **Conclusions** None of the disinfectants were effective when used at manufacturer's recommended concentration for 10 minutes. Phenolic compounds used at 2-4 x the recommended concentration inactivated FCV on contact surfaces. Quarternary ammonium compound and sodium carbonate was effective on contact surfaces at twice the recommended concentration. Rinsing of produce with water reduced virus titer by 2 log_{10}. On artificially contaminated produce, only peroxyacetic acid and hydrogen peroxide were effective when used at 4x manufacturer's recommended concentration for 10 minutes.		
Doultree, J; 1999 [200]	Basic science study N/A	To test glutaraldehyde, iodine, hypochlorite, a quarternary ammonium-based product, an anionic detergent and ethanol for disinfecting activity against FCV. The stability of FCV to	F9 strain of FCV. Study was conducted in Australia.	**Efficacy of disinfectants against FCV** 0.5% glutaraldehyde (Aidal) – complete inactivation Hypochlorite (Det-Sol 5000) – complete inactivation at 1000 and 5000 ppm Hypochlorite (White King) – complete inactivation at 5000 but not at 1000 ppm Quarternary ammonia (Pinocleen) – no reduction 75% ethanol – 1.25 log_{10} reduction 0.8% Iodine (Sanichick) – complete inactivation 1% anionic detergent – 0.5 log_{10} reduction **Heat inactivation of FCV** 56°C – Inactivated at 60 min, no reduction at 1 and 3 min 70°C – Inactivated at 5 min, detected at 1 and 3 min Boiling – Inactivated at 1 min **Survival based on state and temperature** *Suspension*	Complete inactivation represents no detection of FCV	6202_RA

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
		increasing temperature in suspension and in dried state was also tested.		4°C – stable Room temperature – survived for ~20 days 37°C – survived for ~10 days *Dried state* 4°C – stable Room temperature – survived for ~28 days 37°C – survived for ~1-2 days		
Shin, G; 1998 [201]	Basic science study N/A	To test the inactivation of norovirus using monochloramine (2 mg/L in 0.01M phosphate buffer solution at pH 8.0) and compare it to the inactivation of Poliovirus 1 and MS2.	Norovirus from the feces of infected human volunteers. Poliovirus 1 and MS2 viruses as controls. Study was conducted in the US. Not reported	**Reduction in viral titer at 3hr (measured by RT-PCR)** norovirus – 1 $\log_{10}$ Poliovirus 1 – 0 MS2 – 0 However, infectivity assays showed 1 $\log_{10}$ reductions in Poliovirus 1 and MS2 at 3h		6200_RA
Medications						
Rossignol, JF; 2006 [202]	Randomized Controlled Trial 1,3,5,7,9	To evaluate nitazoxanide 500mg vs placebo given to adults or adolescents twice daily for 3 days for the resolution of symptoms due to viral gastroenteritis.	Patients at least 12 years of age with gastroenteritis presenting to outpatient clinics at a university hospital in Egypt. 50 outpatients.	**Symptoms** Nausea in patients with norovirus vs other viral infections – 6/13 (46%) vs 1/32 (3%); p=0.0013 **Time from first dose to symptom resolution** *All results nitazoxanide vs placebo in days (IQR); p value* Overall – 1.5 (0.5-2.5) vs 2.5 (1.5-4.5); <0.0001 For Rotavirus infection – 1.5 (0.5-1.5) vs 2.5 (1.5->6.5);0.0052 For norovirus infection – 1.5 (1.5-1.5) vs 2.5 (1.5-6.5); 0.0295	Patients with diarrhea (≥3 diarrheal stools per day) and stool-positive for rotavirus, norovirus, or adenovirus were eligible for enrollment. Outcome was resolution for at least 72 hours of all symptoms of viral gastroenteritis that were present at	212_IL

Author, Yr (Reference)	Study Design Quality	Study Objective	Population and Setting N	Results	Comments	Ref ID_Data extracted by
					enrollment. A sample size of 19 patients per group, with a 0.05 level two-sided log-rank test for equality of survival curves, had 80% power to detect a difference between an 85% response rate for 1 group and a 40% response rate for a second group at a given time. A sample size of 25 patients per group allowed for exclusion of up to 20% due to other identified causes of diarrhea.	
Gustafson, TL; 1983 [203]	Retrospective controlled study 1,2,3,4	To determine whether certain medications protected patients from symptomatic disease during a norovirus outbreak.	Patients and staff in a chronic-care hospital in Tennessee. Cases – 22 employees and 31 patients. Controls – 14 employees and 25 patients.	**Cases** 55% of elderly psychiatric patients and 61% of nursing employees. **Protective medications** *Attack rates; p values* Patients only on antipsychotic drugs vs on antipsychotic drugs plus trihexyphenidyl or benztropine – 71% vs 14%; 0.013 Patients on psyllium hydrophilic mucilloid vs not receiving psyllium: 27% vs 71%; 0.012	Two case definitions used: For hospital personnel – any person with vomiting or diarrhea (≥1 liquid stools/ day), or two of the following symptoms (abdominal pain, abdominal cramps, or nausea). For patients – any patient with vomiting or diarrhea. Power and sample size not reported.	2014_IL

GRADE TABLE Q3 WHAT PATIENT INTERVENTIONS BEST PREVENT OR CONTAIN NOROVIRUS OUTBREAKS IN THE HEALTHCARE SETTING?

Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**	Large Magnitude**	Dose-response	Confounders		
Virus Shedding														
Virus shedding	Duration of shedding	2 DES [149,150]	78% of infected cases were shedding virus on day 1 compared to 26% on day 22 in 1 DES [149]. The rate was highest in newborns An elderly woman shed norovirus on day 2 and day 5 after resolution of symptoms [150]	High	0	0	0	-1	0	0	0	0	Moderate	-
	Factors associated with shedding	1 OBS [148] 1 DES [149]	Age ≤ 6 months was a possible risk factor when compared with age > 1 year for increased viral shedding in 1 OBS [148] The rate was highest in newborns 1 DES [149]	Low	0	0	0	0	0	0	0	0	Low	
	Asymptomatic shedding	3 DES [150-152]	Asymptomatic shedding was reported in 3 DES [150-152]	High	0	0	0	0	0	0	0	0	High	
Recovery of norovirus														
Fomites	Transfer of norovirus*	1 BAS [194]	One BAS demonstrated that norovirus-contaminated surfaces can be readily transferred to other fomites (telephones, taps, door handles) via fingertips even when virus has been left to dry for 15 minutes in 30-50% of opportunities [194]	High	0	0	-1	-1	0	0	0	0	Low	Low
	Duration of Recovery	1 SR [153] of DES 1 OBS[141]	norovirus remained viable in carpets up to 12 days despite regular vacuuming in 1 SR [153] norovirus was undetectable in areas of previously known contamination after 5 months had elapsed [141]	Low	0	0	0	0	0	0	0	0	Low	

Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**	Large Magnitude**	Dose-response	Confounders		
	Location of norovirus/ FCV Recovery	1 SR [153] of DES 7 DES [154-159,161] 1 BAS [163]	36% of swabs were positive from curtains, cushions, carpets, lockers, commodes, toilet rims, seats and handles, taps, basins, telephones, door handles, physiotherapy instrument handles, and horizontal surfaces above 1.5 meters (i.e., mantle piece and light fittings where direct handling is unlikely) and below 1.5 meters (i.e., tables and ledges where direct handling may occur) in 1 SR [153] Other environmental surfaces identified were bathroom surfaces like toilet seats, handrails and taps; horizontal surfaces near toilets like tables, mantel pieces, light fittings; kitchen surfaces like dining room tables; elevator buttons; bed rails; doorknobs; game consoles; instrument handles (e.g., ultrasound); soft furnishings like cushions and curtains; lockers [154,155,157-159,161] FCV was recovered from computer keyboard and mouse; telephone buttons, receiver and wire in 1 DES [156]	High	0	-1	0	0	0	0	0	0	Moderate	
Foods and food preparation surfaces	Location of norovirus Recovery	3 BAS [112,162,163]	Norovirus was transferred via gloved hands and detected on foods like lettuce, strawberry and ham. norovirus was also detected on food preparation surfaces like stainless steel, ceramic and formica surfaces; spatula; fork; cutting board [112,162,163]	High	0	0	-1	0	0	0	0	0	Moderate	Low
	Transfer of norovirus*	2 BAS [162,163]	Significantly higher transfer to wet lettuce (P<0.01). For dry lettuce, the transfer at time 0 was statistically significantly higher than at times 30 and 60 min (P<0.05). For wet lettuce, the transfer at time 0 was statistically significantly higher than at times 10, 30 and 60 min (P<0.05) [162] Transferred via gloved hands in 1 BAS [163]	High	-0	0	-1	-1	0	0	0	0	Low	
	Factors associated with recovery	1 BAS [112]	In 1 BAS [112], its recovery on ham was significantly greater when compared to other food and surface items.	High	-0	0	-1	-1	0	0	0	0	Low	

Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**	Large Magnitude**	Dose-response	Confounders		
	Duration of Recovery	2 BAS [112,162]	At room temperature and 4ºC, FCV titers were significantly reduced by Day 7 in 1 BAS [112] norovirus was detected on all plated sterile surfaces, with the most significant reduction in titer occurring after 24hrs without cleaning or disinfection. Over 7 days, observed 6-7 log10 reduction in recovery in 1 BAS [162]	High	0	0	-1	0	0	0	0	0	Moderate	
Water	Recovery of norovirus	3 DES [155,158,160]	norovirus was detected in water samples in 1 DES [160]and not detected in 2 DES [155,158]	High	0	0	0	-1	0	0	0	0	Moderate	-
Components of an Outbreak Prevention/Containment Program														
Hand hygiene														
Soap and water	Symptomatic norovirus infection*	1 OBS [66] 18 DES [63,79,85,89,102,103,165,166,168-171,174-177,183,205]	Handwashing was not associated with a significantly decreased risk in 1 OBS [66] Emphazised as an intervention in 17 DES [63,79,85,89,102,103,165,166,168-171,174-177,183,205]. Involved wetting hands, using liquid soap, scrubbing 15 seconds, rinsing with water, and drying hands with a disposable paper towel in 1 DES in the healthcare setting [174]. Guests were encouraged to wash hands after using the bathroom and prior to each meal in 1 DES at a mother and child health clinic [63]. Hygiene measures were implemented without waiting for virological confirmation in 1 DES in the healthcare setting [175]	Low	0	0	0	-1	0	0	0	0	Very Low	Very Low

Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**	Large Magnitude**	Dose-response	Confounders		
Alcohol-based hand sanitizers	Symptomatic norovirus infection*	4 DES [87,169,171,205]	Mandatory hand disinfection with a product that has 95% ethanol in 2 DES in the healthcare setting [169,171] 70% alcohol handrub supplemented by routine handwashing in 1 DES [87] Alcohol based handrubs were available by every bedside in 1 DES in the healthcare setting [205]	Very Low	0	0	0	0	0	0	0	0	Very Low	Very Low
	Inactivation of FCV	4 BAS [189,191,193,196]	Ethanol was found to be superior to propanol as a handwashing agent in 2 BAS [193,196] A new disinfectant with reduced ethanol content was more efficacious that ethanol and propranolol in 1 BAS [189]	High	0	0	-1	0	0	0	0	0	Moderate	
Artificial nails	Inactivation of FCV	1 BAS [197]	1 BAS concluded that food handlers should refrain from using artificial fingernails, keep fingernails short, and scrub with soap and nailbrush when washing hands [197]	Low	0	0	-1	0	0	0	0	0	Very Low	-
PPE														
PPE	Symptomatic norovirus infection*	1 OBS [66] 13 DES [167-172,176-179,181,183,205]	Wearing gowns was not associated with a significantly decreased risk among nursing staff in 1 OBS [66] Protective apparel like masks, gloves, gowns for staff especially when in contact with symptomatic patients were emphazised as an intervention in 13 DES [167-172,176-179,181,183,205] Protective apparel were recommended for both staff and visitors in 2 DES [169,179]	Low	0	0	0	-1	0	0	0	0	Very Low	Very Low
Leave policies for staff														
Leave policies for staff	Symptomatic norovirus infection*	17 DES [84,85,92,165,167-169,172,174,176,177,179-181,183,184,205]	Emphazised as an intervention in 17 DES [84,85,92,165,167-169,172,174,176,177,179-181,183,184,205]	Very Low	0	0	0	0	0	0	0	0	Very Low	Very Low

Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**	Large Magnitude**	Dose-response	Confounders		
			Staff were excluded from work until symptom free for 24 hours in 1 DES [85] Staff were excluded from work until symptom free for 48 hours in 11 DES [84,92,167,169,172,176,177,179,180,183,184] Staff were excluded from work until symptom free for 72 hours in 1 DES [168]											
Isolation/cohorting of symptomatic patients														
Isolation of affected patients	Symptomatic norovirus infection*	15 DES [87,166-171,176,177,179-182,184,205]	Emphasized as an intervention in 15 DES [87,166-171,176,177,179-182,184,205] In 1 DES that provided detailed description of the intervention, all symptomatic patients were isolated, while those who remained asymptomatic were kept in the original ward and isolated only when they subsequently developed clinical symptoms [170]	Very Low	0	0	0	0	0	0	0	0	Very Low	Very Low
Staff cohorting														
Staff cohorting	Symptomatic norovirus infection*	13 DES [87,103,165,168-170,172,177,179,180,182,183,205]	Emphasized as an intervention in 13 DES [87,103,165,168-170,172,177,179,180,182,183,205] Nurses on affected floors cohorted in 1 DES - one group cared for symptomatic patients and a second group for asymptomatic patients [168] Essential medical and paramedical staff who worked in affected ward were not allowed to work in unaffected clinical areas and non-essential personnel were not allowed to enter the affected ward in 1 DES [170] Staff without symptoms working in affected ward did not work anywhere else until 48 hours after completion of work in affected ward	Very Low	0	0	0	0	0	0	0	0	Very Low	Very Low

Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**	Large Magnitude**	Dose-response	Confounders		
			in 1 DES [177]											
Ward closure														
Ward closure	Symptomatic norovirus infection*	1 OBS [164] 11 DES [85,165,166,168,176-179,183,184,205]	Emphasized as an intervention in 1 OBS [164] and 11 DES [85,165,166,168,176-179,183,184,205] Outbreaks were contained significantly sooner when units were closed to new admissions within 4 days in 1 OBS [164] Hospital was closed 6 days after outbreak initiation until 4 days after the last case was symptom free in 1 DES [184] A hotel was closed for 8 h to permit thorough cleaning of all food service areas and guest rooms in 1 DES. New guests were not accepted until all guestrooms, bathrooms, and common rooms were thoroughly cleaned 7 days after initial cases [85]	Low	0	0	0	-1	0	1	0	0	Low	Low
Visitor policies														
Visitor policies	Symptomatic norovirus infection*	5 DES [168,170,182,183,205]	Restriction of visitors was emphasized as an intervention in 5 DES [168,170,182,183,205] Nurse managers screened all visitors for gastroenteritis, and if symptomatic, prohibited them from visiting patients in the units for 72 hours in 1 DES [168] Visitors were restricted to the immediate family and children were restricted from visiting in 1 DES [183] Visitors were restricted to two for each patient in 1 DES. All visitors were registered and records were kept for 14 days. All visitors were screened by a standard questionnaire for symptoms and signs of gastroenteritis [170] Visitors were restricted to one unit per visit in 1 DES [182]	Very Low	0	0	0	0	0	0	0	0	Very Low	Very Low

Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**	Large Magnitude**	Dose-response	Confounders		
Education														
Education	Symptomatic norovirus infection*	6 DES [166,168,169,172,182,205]	Education of healthcare workers was emphasized as an intervention in 5 DES [166,168,169,182,205] Possible topics included identification of norovirus, spread of gastroenteritis, cleaning and disinfection procedures, isolation, transfers, discharge. Education was provided to family members in 1 DES [172]	Very Low	0	0	0	0	0	0	0	0	Very Low	Very Low
Surveillance														
Surveillance	Symptomatic norovirus infection*	4 DES [58,84,166,170]	Emphasized as an intervention in 4 DES [58,84,166,170] Active surveillance and case finding after defining the surveillance period and establishing a case definition was recommended in 1 DES. Contact tracing among staff was done and admission records of patients were reviewed[170] Active surveillance was promoted using a two-tiered definition of cases and outbreaks in 1 DES [58]	Very Low	0	0	0	0	0	0	0	0	Very Low	Very Low
Policy Development and Communication														
Policy development and communication	Symptomatic norovirus infection*	6 DES [63,84,172,182-184]	Emphasized as an intervention in 6 DES [63,84,172,182-184]	Very Low	0	0	0	0	0	0	0	0	Very Low	Very Low
Patient Transfers and Discharges														
Patient discharges	Symptomatic norovirus infection*	4 DES [172,179,183,184]	Transfer of patients after symptom resolution was supported in 1 DES [172], but discouraged in 3 DES [179,183,184] unless medically necessary.	Very Low	0	0	0	0	0	0	0	0	Very Low	Very Low
Environmental Disinfection														
Targeted surface disinfection	Symptomatic norovirus	1 SR [153] of DES 3 DES [79,168,183]	Emphasized as an intervention in 1 SR [153] and 3 DES [79,168,183] for high touch surfaces (eg. patient and staff bathrooms and clean/dirty	Very Low	0	0	0	0	0	0	0	0	Very Low	Very Low

Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**	Large Magnitude**	Dose-response	Confounders		
	infection*		utility rooms, tables, chairs, commodes, computer keyboards/mice, and items in close proximity to symptomatic patients) and carpets											
Process of environmental disinfection	Symptomatic norovirus infection*	4 DES [168,170,177,179]	The frequency of routine ward, bathroom and toilet cleaning was increased to hourly and hypochlorite was used to disinfect hard surfaces after cleaning in 1 DES [179] Diluted sodium hypochlorite was used for all horizontal surfaces and toilets were cleaned three times daily in 1 DES [177] The routine cleansing of ward was increased to twice daily in 1 DES [170] Mop heads were changed every 3 rooms in 1 study [168]	Very Low	0	0	0	0	0	0	0	0	Very Low	Very Low
Cleaning/ disinfection of patient service items	Symptomatic norovirus infection*	3 DES [168,172,177]	Emphasized as an intervention in 3 DES [168,172,177]	Very Low	0	0	0	0	0	0	0	0	Very Low	Very Low
Cleaning/ disinfection of fabrics	Symptomatic norovirus infection*	1 SR [153] of DES 3 DES [168,177,183]	Changing patient curtains if visibly soiled in 1 SR [153] and 2 DES [168,177] One DES suggested that soiled, upholstered patient equipment should be steam cleaned. If this was not possible, these items were discarded [168] Careful handling of soiled linen to minimize re-aerosolization of virus in 2 DES [177,183]	Very Low	0	0	0	0	0	0	0	0	Very Low	Very Low

Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**	Large Magnitude**	Dose-response	Confounders		
Cleaning and disinfection agents	Symptomatic norovirus infection*	1 SR [153] of 14 DES [63,83,87,89,167,168,170,174,176-179,182,184]	Emphasized as an intervention in 1 SR [153] and 12 DES [63,83,167,168,170,174,176-179,182,184] In one DES, concentrated hypochlorite (1000 ppm) was used for disinfection. The frequency of routine cleaning of the ward was increased and the cleansing area was widened to one square meter surrounding the infected area [170] Hypochlorite was used to disinfect hard surfaces after cleaning in 1 DES [179] 1% sodium hypochlorite was used to wipe down surfaces for spills of vomitus and feces, thorough facility wide cleaning was performed, all continence pads treated as infectious waste and additional mop heads allocated to all the units in 1 DES [182] Diluted sodium hypochlorite was used for all horizontal surfaces in 1 DES [177] Rooms were disinfected with 0.5% hypochlorite after patient discharge in 1 DES [167] Rooms were cleaned with 1% aldehyde or 0.1% chlorine-free bleach in 1 DES [174] Unit was disinfected several times with 1:10 diluted hypochlorite (household bleach) in 1 DES [176] Hypochlorite was used to disinfect hard surfaces in 1 DES [178] 2% hypochlorite solution used in 2 DES [87,89] Cleaning regimen used hypochlorite solution and alcohol wipes in 1 DES [184] An outbreak resulted when vomiting was cleaned with an ordinary vacuum cleaner without hypochlorite [83]	Very Low	0	0	0	0	0	0	0	0	Very Low	Very Low

Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**	Large Magnitude**	Dose-response	Confounders		
	Inactivation of norovirus*	3 BAS [187,194,201]	5% organic acid, 1% peroxide, not less than 2% aldehyde with a contact time of 1 h or a 1% halogen compound with 6,000 ppm of free chlorine and a contact time of 15 minutes were required for safe disinfection in 1 BAS [187] Cleaning a contaminated surface with a cloth soaked in anionic detergent followed by cleaning with a combination of hypochlorite/detergent was found to the best cleaning regimen in 1 BAS. Cleaning with the detergent alone or the hypochlorite/detergent combination without prior cleaning failed to eliminate norovirus contamination [194] Treatment of water with monochloramine produced negligible reduction in norovirus titer in 1 BAS [201]	High	0	0	-1	0	0	0	0	0	Moderate	

Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**	Large Magnitude**	Dose-response	Confounders		
	Inactivation of FCV	9 BAS [185,187,188,190-192,198-200]	An activated aldehyde based product was found to be the most effective disinfectant on all types of fabric and carpet in 1 BAS [190], although statistical differences were not reported A quarternary ammonium compound exhibited similar efficacy to hypochlorite 1000 ppm in 1 DES [188] Ethanol at 70% and 90% and isopropranol at 40-60% were effective at killing 99% of FCV within 1 min in 1 BAS [191] Sodium bicarbonate at concentrations of 5% and above was found to achieve 99% reduction in FCV titers, both alone and in combination with aldehyde or hydrogen peroxide in 1 BAS [192] FCV was more resistant to UV light when compared with hepatitis A virus, polio virus and round coliphages although statistical differences were not reported in 1 BAS [198] 0.5% glutaraldehyde, hypochlorite and 0.8% iodine completely inactivated FCV, but a quarternary ammonium compound, ethanol and a 1% anionic detergent did not in 1 BAS [200] 4% organic acid, 1% peroxide, not less than 2% aldehyde with a contact time of 1 h or a 1% halogen compound with 6,000 ppm of free chlorine and a contact time of 15 minutes were required for safe disinfection in 1 BAS [187] 1 BAS demonstrated that ozone from a portable commercial generator could inactivate norovirus and FCV [185] Phenolic compounds, peroxyacetic acid + hydrogen peroxide, and quarternary ammonium compound + sodium bicarbonate were effective at concentrations 2-4 times that recommended by the manufacturers in 1 BAS [199]	High	0	0	-1	0	0	0	0	0	Moderate	

Comparison	Outcome	Quantity and type of evidence	Findings	Starting grade	Decrease GRADE					Increase GRADE			GRADE of Evidence for Outcome	Overall GRADE of Evidence Base
					Study Quality**	Consistency**	Directness**	Precision**	Publication Bias**	Large Magnitude**	Dose-response	Confounders		
Medications														
Medications	Symptomatic norovirus infection*	1 OBS [203]	Psychiatric patients who received trihexyphenidyl or benztropine in addition to antipsychotic drugs had a significantly decreased risk compared to those who received antipsychotic drugs alone Patients who received psyllium had a significantly decreased risk compared with those who did not.	Low	0	0	0	-1	0	0	0	0	Very Low	Very Low
	Time to symptom resolution*	1 RCT [202]	Significantly decreased in patients who received nitazoxanide when compared to those who did not.	High	0	0	-1	-1	0	0	0	0	Low	

RCT – randomized controlled trial; OBS – observational study (prospective or retrospective controlled); DES – descriptive study (case series, case report, uncontrolled data in an observational study); BAS – basic science study

* These outcomes are considered the most critical by the guideline developers.

** These modifiers can impact the GRADE by 1 or 2 points

APPENDIX 3: DATA EXTRACTION TOOL

Author, Yr (Reference)

Study Design

Study Objective

Population and Setting

Power and Sample Size

N

Results

Outcome definitions

Other comments

Relevant Questions: (√ all that apply)

Question 1: Question 2: Question 3: Question 4: Question 5:

QUALITY ASSESSMENT

1. Systematic review

Search terms described
Databases searched described and two or more databases searched
Inclusion/exclusion criteria described
Number of included/excluded studies along with reasons of exclusion described
Studies screened by two independent reviewers for inclusion
Data extracted by two independent reviewers
Individual study quality assessed
Heterogeneity between study results assessed qualitatively and/or quantitatively
Publication bias assessed

2. Randomized controlled trial

Described as randomized
Randomization appropriately performed (e.g. random number table, computerized scheme)
Described as double-blind
Outcome assessor blinded
Study participant blinded (e.g. interventions identical in appearance)
Investigator blinded (e.g. opaque sealed envelopes)
Attrition described
Attrition smaller than 10-15% of assigned patients
Attrition appropriately analyzed (e.g. intention to treat analysis)

3. Prospective/retrospective controlled or pre-post studies

All study groups derived from similar source/reference populations
Attrition not significantly different across study groups
The measure of exposure is valid
The measure of outcome is valid
Investigators blinded to endpoint assessment
Potential confounders identified
Statistical adjustment for potential confounders done

4. Descriptive Study

Valid selection of study sample (consecutive or randomly selected subjects)
Criteria for inclusion/exclusion clearly stated
Outcomes measured in a valid manner
Effect estimates presented (e.g. proportions)

5. Diagnostic study

Valid selection of study sample (consecutive or randomly selected subjects)
Valid reference standard
Diagnostic test and reference standard performed independently in each subject
Diagnostic test and reference standard evaluated independently on each subject (blinding)

6. Economic evaluation

Perspective defined (e.g. societal, payer, provider)
Time horizon defined
Decision tree(s) or rule(s) explicit
Sources of cost estimates presented
Sources of event rate estimates presented
Sensitivity analyses performed

7. Basic science study

N/A

8. Please mention any other relevant quality considerations:

APPENDIX 4: QUALITY CHECKLISTS

I. SYSTEMATIC REVIEW

1. Search terms described
2. Databases searched described and two or more databases searched
3. Inclusion/exclusion criteria described
4. Number of included/excluded studies along with reasons of exclusion described
5. Studies screened by two independent reviewers for inclusion
6. Data extracted by two independent reviewers
7. Individual study quality assessed
8. Heterogeneity between study results assessed qualitatively and/or quantitatively
9. Publication bias assessed

II. RANDOMIZED CONTROLLED TRIAL

1. Described as randomized
2. Randomization appropriately performed (e.g. random number table, computerized scheme)
3. Described as double-blind
4. Outcome assessor blinded
5. Study participant blinded (e.g. interventions identical in appearance)
6. Investigator blinded (e.g. opaque sealed envelopes)
7. Attrition described
8. Attrition smaller than 10-15% of assigned patients
9. Attrition appropriately analyzed (e.g. intention to treat analysis)

III. PROSPECTIVE/RETROSPECTIVE CONTROLLED OR PRE-POST STUDIES

1. All study groups derived from similar source/reference populations
2. Attrition not significantly different across study groups
3. The measure of exposure is valid
4. The measure of outcome is valid
5. Investigators blinded to endpoint assessment
6. Potential confounders identified
7. Statistical adjustment for potential confounders done

IV. Case Series

1. Valid selection of study sample (consecutive or randomly selected subjects)
2. Criteria for inclusion/exclusion clearly stated
3. Outcomes measured in a valid manner
4. Effect estimates presented (e.g. proportions)

V. Case Reports

N/A

VI. Diagnostic study

1. Valid selection of study sample (consecutive or randomly selected subjects)
2. Valid reference standard
3. Diagnostic test and reference standard performed independently in each subject
4. Diagnostic test and reference standard evaluated independently on each subject (blinding)

VII. Economic evaluation

1. Perspective defined (e.g. societal, payer, provider)
2. Time horizon defined
3. Decision tree(s) or rule(s) explicit
4. Sources of cost estimates presented
5. Sources of event rate estimates presented
6. Sensitivity analyses performed

VIII. Basic science study

N/A

References

1. Green KY, Ando T, Balayan, et al. Taxonomy of the caliciviruses. J Infect Dis. 2000;181 (Supplement 2):S322-30.
2. Atmar RL, Estes MK. The epidemiologic and clinical importance of norovirus infection. Gastroenterol Clin North Am. 2006;35(2):275-290.
3. Kaplan JE, Schonberger LB, Varano G, Jackman N, Bied J, Gary GW. An outbreak of acute nonbacterial gastroenteritis in a nursing home. Demonstration of person-to-person transmission by temporal clustering of cases. Am J Epidemiol. 1982;116(6):940-948.
4. Mead PS, Slutsker L, Dietz V, et al. Food-related illness and death in the United States. Emerg Infect Dis. 1999;5(5):607-625.
5. Widdowson MA, Meltzer MI, Zhang X, Bresee JS, Parashar UD, Glass RI. Cost-effectiveness and potential impact of rotavirus vaccination in the United States. Pediatrics. 2007;119(4):684-697.
6. Patel MM, Widdowson MA, Glass RI, Akazawa K, Vinje J, Parashar UD. Systematic literature review of role of noroviruses in sporadic gastroenteritis. Emerg Infect Dis. 2008;14(8):1224-1231.
7. Fankhauser RL, Monroe SS, Noel JS, et al. Epidemiologic and molecular trends of "Norwalk-like viruses" associated with outbreaks of gastroenteritis in the United States. J Infect Dis. 2002;186(1):1-7.
8. Widdowson MA, Cramer EH, Hadley L, et al. Outbreaks of acute gastroenteritis on cruise ships and on land: identification of a predominant circulating strain of norovirus--United States, 2002. J Infect Dis. 2004;190(1):27-36.
9. Siebenga JJ, Vennema H, Zheng DP, et al. Norovirus illness is a global problem: emergence and spread of norovirus GII.4 variants, 2001-2007. J Infect Dis. 2009;200(5):802-812.
10. Centers for Disease Control and Prevention (CDC). Norovirus activity--United States, 2006-2007. MMWR. 2007;56(33):842-846.
11. Centers for Disease Control and Prevention (CDC). Surveillance for foodborne disease outbreaks - United States, 2006. MMWR. 2009;58(22):609-615.
12. Caul EO. Small round structured viruses: airborne transmission and hospital control. Lancet. 1994;343(8908):1240-1242.
13. Hutson AM, Atmar RL, Estes MK. Norovirus disease: changing epidemiology and host susceptibility factors. Trends Microbiol. 2004;12(6):279-287.
14. Donaldson EF, Lindesmith LC, Lobue AD, Baric RS. Norovirus pathogenesis: mechanisms of persistence and immune evasion in human populations. Immunol Rev. 2008;225:190-211.
15. Widerlite L, Trier JS, Blacklow NR, Schreiber DS. Structure of the gastric mucosa in acute infectious bacterial gastroenteritis. Gastroenterology. 1975;68(3):425-430.
16. Kaplan JE, Feldman R, Campbell DS, Lookabaugh C, Gary GW. The frequency of a Norwalk-like pattern of illness in outbreaks of acute gastroenteritis. Am J Public Health. 1982;72(12):1329-1332.
17. Rabenau HF, Sturmer M, Buxbaum S, Walczok A, Preiser W, Doerr HW. Laboratory diagnosis of norovirus: which method is the best?. Intervirology. 2003;46(4):232-238.
18. Trujillo A, McCaustland K, Zheng D, et al. Use of TaqMan real-time reverse transcription-PCR for rapid detection, quantification, and typing of norovirus. Journal of Clinical Microbiology.American Society for Microbiology (ASM), Washington, USA. 2006;44(4):1405-1412. http://dx.doi.org/10.1128/JCM.44.4.1405-1412.2006.
19. Said MA, Perl TM, Sears CL. Healthcare epidemiology: gastrointestinal flu: norovirus in health care and long-term care facilities. Clin Infect Dis. 2008;47(9):1202-1208.

20. Cannon JL, Papafragkou E, Park GW, Osborne J, Jaykus LA, Vinje J. Surrogates for the study of norovirus stability and inactivation in the environment: aA comparison of murine norovirus and feline calicivirus. J Food Prot. 2006;69(11):2761-2765.
21. Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ. 2008;336(7650):924-926.
22. Guyatt GH, Oxman AD, Kunz R, et al. What is "quality of evidence" and why is it important to clinicians? BMJ. 2008;336(7651):995-998.
23. Guyatt GH, Oxman AD, Kunz R, et al. Going from evidence to recommendations. BMJ. 2008;336(7652):1049-1051.
24. Schunemann HJ, Oxman AD, Brozek J, et al. Grading quality of evidence and strength of recommendations for diagnostic tests and strategies. BMJ. 2008;336(7653):1106-1110.
25. Vessel Sanitation Program Construction Guideline, July 2005. Available at: http://www.cdc.gov/nceh/vsp/ConstructionGuidelines/ConstructionGuidelines2005.pdf. Accessed September 24, 2007.
26. Vessel Sanitation Program Operations Manual, August 2005. Available at: http://www.cdc.gov/nceh/vsp/operationsmanual/OPSManual2005.pdf. Accessed September 24, 2007.
27. Guidance for the Management of Norovirus Infection in Cruise Ships. July 2007. Available at: http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1206520183347. Accessed September 24, 2007.
28. Viral Gastroenteritis: Leeds Teaching Hospitals Trust Infection Control Policies. 2008. Available at: http://www.leedsteachinghospitals.com/sites/infection_control/documents/VGrevisedJan08.pdf. Accessed September 24, 2007.
29. National Guidelines on the Management of Outbreaks of Norovirus Infection in Healthcare Settings. 2003. Available at: http://www.hpsc.ie/hpsc/A-Z/Gastroenteric/ViralGastroenteritis/Publications/File,1194,en.pdf. Accessed September 24, 2007.
30. Netherlands: Norovirus Guidelines for Cruiseships and Hotels. 2007. Accessed September 24, 2007.
31. Gastroenteritis in an Institution Response Protocol for New South Wales Public Health Units, NSW Health 2005. (updated 2010). Available at: http://www.health.nsw.gov.au/factsheets/guideline/gastro.html. Accessed September 24, 2007.
32. Guidelines for the Management of Norovirus Outbreaks in Hospitals and Elderly Care Institutions, July 2007, Auckland Regional Public Health Service, New Zealand. (updated 2008). Available at: http://www.arphs.govt.nz/notifiable/downloads/Norovirus_Guidelines_2008.pdf. Accessed September 24, 2007.
33. Viral Gastroenteritis Outbreaks: Information for Supervisors in the Child Care and Hospitality Industries. Queensland Health, Australia. (updated 2010). Available at: http://www.health.qld.gov.au/ph/documents/cdb/26888.pdf. Accessed September 24, 2007.
34. Aide-Memoire for Managing Norovirus Outbreaks in Healthcare Settings Scottish Centre for Infection and Environmental Health, National Services Scotland. 2004. Available at: http://www.hps.scot.nhs.uk/giz/publicationsdetail.aspx?id=22582. Accessed September 24, 2007.
35. The Identification and Management of Outbreaks of Norovirus Infection in Tourists and Leisure Industry Settings. 2005. Available at: http://www.sefton.gov.uk/pdf/epd_norovirusguide.pdf. Accessed September 24, 2007.
36. Guidelines for the Management of Infectious Gastroenteritis in Aged Care Facilities in South Australia. 2005. Available at: http://www.publications.health.sa.gov.au/cgi/viewcontent.cgi?article=1014&context=cdc. Accessed September 24, 2007.
37. General Guidelines for the Management of Viral Gastroenteritis, Community Infection Prevention and Control Policy and Procedure, Gloucestershire Primary Care Trust, 2008. Available at: http://www.glospct.nhs.uk/pdf/policies/infectioncontrol/gpct%20viral%20gastroenteritis.pdf. Accessed September 24, 2007.

38. Recommendations for the Prevention and Control of Viral Gastroenteritis Outbreaks in California Long-Term Care Facilities. 2006 Available at: http://www.cdph.ca.gov/pubsforms/Guidelines/Documents/PCofViralGastroenteritisOutbreaks.pdf. Accessed September 24, 2007.
39. Control of Viral Gastroenteritis Outbreaks in Illinois Long-Term Care Facilities. Illinois Department of Public Health. 2006. Available at: http://www.co.mchenry.il.us/departments/health/pdfDocs/PHS/CD/NoroLongFacGuide.pdf. Accessed September 24, 2007.
40. Norovirus Prevention Guidance for Institutions/Facilities. Virginia Department of Health, January 2007. Available at: http://www.flpic.com/Norovirus_Prev_Guidance_Institutions_2007.pdf. Accessed September 24, 2007.
41. Viral Gastroenteritis Outbreak Guidelines for Child Care Facilities. Washoe County District Health Department, Reno, Nevada. http://www.co.washoe.nv.us/repository/files//4/Childcare_guidelines_for_norovirus.pdf. Accessed September 24, 2007
42. Viral Gastroenteritis Outbreak Guidelines for Community Living Facilities. Washoe County District Health Department, Reno, Nevada. 2005. Available at: http://www.co.washoe.nv.us/repository/files/4/Guidelines%20for%20Norovirus%20in%20ECFs.pdf. Accessed September 24, 2007.
43. Guidelines for the Epidemiological Investigation of Gastroenteritis Outbreaks in Long Term Care Facilities, Maryland Department of Health and Mental Hygiene. Revised 2001. Available at: http://ideha.dhmh.maryland.gov/pdf/guidelines/gastroenteritis.aspx. Accessed September 24, 2007.
44. Recommendations for the Control of Viral Gastroenteritis Outbreaks in Long-Term Care Facilities and Viral Gastroenteritis Outbreaks in Nursing Homes or Long-Term Care Facilities Guidelines for Environmental Decontamination. Georgia Department of Community Health. Available at: http://health.state.ga.us/pdfs/epi/notifiable/outbreaks/Norovirus%20cleaning%20guidelines_LTC.pdf. Accessed September 24, 2007.
45. Recommendations for the Prevention and Control of Viral Gastroenteritis Outbreaks in Wisconsin Long-Term Care Facilities. Wisconsin Division of Public Health. (updated 2009). Available at: http://www.dhs.wisconsin.gov/rl_dsl/Providers/norovirusRecoLTCF09.pdf. Accessed September 24, 2007.
46. Norovirus (Viral Gastroenteritis) Control Measures for Skilled Nursing Facilities. Los Angeles County Public Health. 2006. Available at: http://www.publichealth.lacounty.gov/acd/docs/Norovirus/NorovirusControlMeasures_12_1_06.pdf. Accessed September 24, 2007.
47. Norovirus (Viral Gastroenteritis): Information Packet for Nursing Facilities. Washington State Department of Health, May 2005. Available at: http://www.co.thurston.wa.us/health/personalhealth/communicabledisease/DrYuUpdates/PDF/2011noropacket.pdf. Accessed September 24, 2007.
48. Viral Gastroenteritis Guidance. Royal Devon and Exeter. NHS, August 2007. (revised July 2009). Available at: http://www.rdehospital.nhs.uk/docs/patients/services/infection_control/Viral%20gastroenteritis-Aug2009.pdf. Accessed September 24, 2007.
49. Norovirus Infections. Public Health Importance and Outbreak Management. Public Health-Seattle and King County. Updated March 2010. Available at: http://www.kingcounty.gov/healthservices/health/communicable/diseases/NorovirusControl.aspx. Accessed September 24, 2007.
50. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Ann Intern Med. 2007;147(8):573-577.
51. Shea BJ, Grimshaw JM, Wells GA, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Med Res Methodol. 2007;7:10.
52. Sanderson S, Tatt ID, Higgins JP. Tools for assessing quality and susceptibility to bias in observational studies in epidemiology: a systematic review and annotated bibliography. Int J Epidemiol. 2007;36(3):666-676.

53. Moher D, Schulz KF, Altman D, CONSORT Group (Consolidated Standards of Reporting Trials). The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomized trials. JAMA. 2001;285(15):1987-1991.
54. Jadad AR, Moore RA, Carroll D, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? Control Clin Trials. 1996;17(1):1-12.
55. Yale Center for Medical Informatics. 2009. Available at: http://ycmi.med.yale.edu/. Accessed April 27, 2011.
56. Mattner F, Mattner L, Borck HU, Gastmeier P. Evaluation of the impact of the source (patient versus staff) on nosocomial norovirus outbreak severity. Infect Control Hosp Epidemiol. 2005;26(3):268-272.
57. Mattner F, Sohr D, Heim A, Gastmeier P, Vennema H, Koopmans M. Risk groups for clinical complications of norovirus infections: an outbreak investigation. Clin Microbiol Infect. 2006;12(1):69-74.
58. Lopman BA, Reacher MH, Vipond IB, Sarangi J, Brown DW. Clinical manifestation of norovirus gastroenteritis in health care settings. Clin Infect Dis. 2004;39(3):318-324.
59. Lee N, Chan MCW, Wong B, et al. Fecal viral concentration and diarrhea in norovirus gastroenteritis. Emerg Infect Dis. 2007;13(9):1399-1401. http://www.cdc.gov/eid/content/13/9/pdfs/1399.pdf.
60. Rodriguez-Guillen L, Vizzi E, Alcala AC, Pujol FH, Liprandi F, Ludert JE. Calicivirus infection in human immunodeficiency virus seropositive children and adults. J Clin Virol. 2005;33(2):104-109.
61. de Wit MA, Koopmans MP, van Duynhoven YT. Risk factors for norovirus, Sapporo-like virus, and group A rotavirus gastroenteritis. Emerg Infect Dis. 2003;9(12):1563-1570.
62. Gotz H, Ekdahl K, Lindback J, de Jong B, Hedlund KO, Giesecke J. Clinical spectrum and transmission characteristics of infection with Norwalk-like virus: findings from a large community outbreak in Sweden. Clin Infect Dis. 2001;33(5):622-628.
63. Oppermann H, Mueller B, Takkinen J, Klauditz W, Schreier E, Ammon A. An outbreak of viral gastroenteritis in a mother-and-child health clinic. Int J Hyg Environ Health. 2001;203(4):369-373.
64. Sharp TW, Hyams KC, Watts D, et al. Epidemiology of Norwalk virus during an outbreak of acute gastroenteritis aboard a US aircraft carrier. J Med Virol. 1995;45(1):61-67.
65. Thea DM, Glass R, Grohmann GS, et al. Prevalence of enteric viruses among hospital patients with AIDS in Kinshasa, Zaire. Trans R Soc Trop Med Hyg. 1993;87(3):263-266.
66. Marx A, Shay DK, Noel JS, et al. An outbreak of acute gastroenteritis in a geriatric long-term-care facility: combined application of epidemiological and molecular diagnostic methods. Infect Control Hosp Epidemiol. 1999;20(5):306-311.
67. Caceres VM, Kim DK, Bresee JS, et al. A viral gastroenteritis outbreak associated with person-to-person spread among hospital staff. Infect Control Hosp Epidemiol. 1998;19(3):162-167.
68. Cegielski JP, Msengi AE, Miller SE. Enteric viruses associated with HIV infection in Tanzanian children with chronic diarrhea. Pediatr AIDS HIV Infect. 1994;5(5):296-299.
69. Halperin T, Vennema H, Koopmans M, et al. No association between histo-blood group antigens and susceptibility to clinical infections with genogroup II norovirus. J Infect Dis. 2008;197(1):63-65.
70. Hutson AM, Airaud F, LePendu J, Estes MK, Atmar RL. Norwalk virus infection associates with secretor status genotyped from sera. J Med Virol. 2005;77(1):116-120.

71. Thorven M, Grahn A, Hedlund KO, et al. A homozygous nonsense mutation (428G-->A) in the human secretor (FUT2) gene provides resistance to symptomatic norovirus (GGII) infections. J Virol. 2005;79(24):15351-15355.
72. Lindesmith L, Moe C, Marionneau S, et al. Human susceptibility and resistance to Norwalk virus infection. Nat Med. 2003;9(5):548-553.
73. Hutson AM, Atmar RL, Graham DY, Estes MK. Norwalk virus infection and disease is associated with ABO histo-blood group type. J Infect Dis. 2002;185(9):1335-1337.
74. Graham DY, Jiang X, Tanaka T, Opekun AR, Madore HP, Estes MK. Norwalk virus infection of volunteers: new insights based on improved assays. J Infect Dis. 1994;170(1):34-43.
75. Nakata S, Chiba S, Terashima H, Yokoyama T, Nakao T. Humoral immunity in infants with gastroenteritis caused by human calicivirus. J Infect Dis. 1985;152(2):274-279.
76. Parrino TA, Schreiber DS, Trier JS, Kapikian AZ, Blacklow NR. Clinical immunity in acute gastroenteritis caused by Norwalk agent. N Engl J Med. 1977;297(2):86-89.
77. Fretz R, Svoboda P, Schorr D, Tanner M, Baumgartner A. Risk factors for infections with Norovirus gastrointestinal illness in Switzerland. Eur J Clin Microbiol Infect Dis. 2005;24(4):256-261.
78. Meyer E, Ebner W, Scholz R, Dettenkofer M, Daschner FD. Nosocomial outbreak of norovirus gastroenteritis and investigation of ABO histo-blood group type in infected staff and patients. J Hosp Infect. 2004;56(1):64-66.
79. Centers for Disease Control and Prevention (CDC). Norovirus outbreak in an elementary school--District of Columbia, February 2007. MMWR. 2008;56(51-52):1340-1343.
80. Centers for Disease Control and Prevention (CDC). Multistate outbreak on norovirus gastroenteritis among attendees at a family reunion -- Grant County, West Virginia, October 2006. MMWR. 2007;56(27):673-678.
81. Costas L, Vilella A, Llupia A, Bosch J, Jimenez de Anta MT, Trilla A. Outbreak of norovirus gastroenteritis among staff at a hospital in Barcelona, Spain, September 2007. Euro Surveill. 2007;12(11):E071122.5.
82. Lopman BA, Andrews N, Sarangi J, Vipond IB, Brown DW, Reacher MH. Institutional risk factors for outbreaks of nosocomial gastroenteritis: survival analysis of a cohort of hospital units in South-west England, 2002-2003. J Hosp Infect. 2005;60(2):135-143.
83. Evans MR, Meldrum R, Lane W, et al. An outbreak of viral gastroenteritis following environmental contamination at a concert hall. Epidemiol Infect. 2002;129(2):355-360.
84. Lachlan M, Licence K, Oates K, Vaughan S, Hill R. Practical lessons from the management of an outbreak of small round structured virus (Norwalk-like virus) gastroenteritis. Commun Dis Public Health. 2002;5(1):43-47.
85. Love SS, Jiang X, Barrett E, Farkas T, Kelly S. A large hotel outbreak of Norwalk-like virus gastroenteritis among three groups of guests and hotel employees in Virginia. Epidemiol Infect. 2002;129(1):127-132.
86. Anderson AD, Garrett VD, Sobel J, et al. Multistate outbreak of Norwalk-like virus gastroenteritis associated with a common caterer. Am J Epidemiol. 2001;154(11):1013-1019.
87. Cunney RJ, Costigan P, McNamara EB, et al. Investigation of an outbreak of gastroenteritis caused by Norwalk-like virus, using solid phase immune electron microscopy. J Hosp Infect. 2000;44(2):113-118.
88. Marks PJ, Vipond IB, Carlisle D, Deakin D, Fey RE, Caul EO. Evidence for airborne transmission of Norwalk-like virus (NLV) in a hotel restaurant. Epidemiol Infect. 2000;124(3):481-487.

89. Lo SV, Connolly AM, Palmer SR, Wright D, Thomas PD, Joynson D. The role of the pre-symptomatic food handler in a common source outbreak of food-borne SRSV gastroenteritis in a group of hospitals. Epidemiol Infect. 1994;113(3):513-521.
90. Patterson T, Hutchings P, Palmer S. Outbreak of SRSV gastroenteritis at an international conference traced to food handled by a post-symptomatic caterer. Epidemiol Infect. 1993;111(1):157-162.
91. Alexander WJ, Holmes JR, Shaw JF, Riley WE, Roper WL. Norwalk virus outbreak at a college campus. South Med J. 1986;79(1):33-36.
92. Wit MA, Widdowson V, H., Bruin Ed, Fernandes T, Koopmans M. Large outbreak of norovirus: the baker who should have known better. Journal of Infection. Elsevier, Amsterdam, Netherlands. 2007;55(2):188-193.
93. Centers for Disease Control and Prevention (CDC). Norovirus outbreak associated with ill food-service workers--Michigan, January-February 2006. MMWR. 2007;56(46):1212-1216.
94. Rizzo C, Di Bartolo I, Santantonio M, et al. Epidemiological and virological investigation of a Norovirus outbreak in a resort in Puglia, Italy. BMC Infect Dis. 2007;7:135.
95. Schmid D, Stuger HP, Lederer I, et al. A foodborne norovirus outbreak due to manually prepared salad, Austria 2006. Infection. 2007;35(4):232-239.
96. Payne J, Hall M, Lutzke M, Armstrong C, King J. Multisite outbreak of norovirus associated with a franchise restaurant - Kent County, Michigan, May 2005. MMWRt. 2006;55(14):395-397.
97. Grotto I, Huerta M, Balicer RD, et al. An outbreak of norovirus gastroenteritis on an Israeli military base. Infection. 2004;32(6):339-343.
98. Marks PJ, Vipond IB, Regan FM, Wedgwood K, Fey RE, Caul EO. A school outbreak of Norwalk-like virus: evidence for airborne transmission. Epidemiol Infect. 2003;131(1):727-736.
99. Stegenga J, Bell E, Matlow A. The role of nurse understaffing in nosocomial viral gastrointestinal infections on a general pediatrics ward. Infect Control Hosp Epidemiol. 2002;23(3):133-136.
100. Becker KM, Moe CL, Southwick KL, MacCormack JN. Transmission of Norwalk virus during football game. N Engl J Med. 2000;343(17):1223-1227.
101. Parashar UD, Dow L, Fankhauser RL, et al. An outbreak of viral gastroenteritis associated with consumption of sandwiches: implications for the control of transmission by food handlers. Epidemiol Infect. 1998;121(3):615-621.
102. McEvoy M, Blake W, Brown D, Green J, Cartwright R. An outbreak of viral gastroenteritis on a cruise ship. Commun Dis Rep CDR Rev. 1996;6(13):R188-92.
103. Chadwick PR, McCann R. Transmission of a small round structured virus by vomiting during a hospital outbreak of gastroenteritis. J Hosp Infect. 1994;26(4):251-259.
104. Reid JA, Caul EO, White DG, Palmer SR. Role of infected food handler in hotel outbreak of Norwalk-like viral gastroenteritis: implications for control. Lancet. 1988;2(8606):321-323.
105. Iversen AM, Gill M, Bartlett CL, Cubitt WD, McSwiggan DA. Two outbreaks of foodborne gastroenteritis caused by a small round structured virus: evidence of prolonged infectivity in a food handler. Lancet. 1987;2(8558):556-558.
106. White KE, Osterholm MT, Mariotti JA, et al. A foodborne outbreak of Norwalk virus gastroenteritis. Evidence for post-recovery transmission. Am J Epidemiol. 1986;124(1):120-126.
107. Kaplan JE, Gary GW, Baron RC, et al. Epidemiology of Norwalk gastroenteritis and the role of Norwalk virus in outbreaks of acute nonbacterial gastroenteritis. Ann Intern Med. 1982;96(6 Pt 1):756-761.

108. Tu ETV, Bull RA, Greening GE, et al. Epidemics of gastroenteritis during 2006 were associated with the spread of norovirus GII.4 variants 2006a and 2006b. Clinical Infectious Diseases. 2008;46(3):413-420.
109. Adamson WE, Gunson RN, Maclean A, Carman WF. Emergence of a new norovirus variant in Scotland in 2006. J Clin Microbiol. 2007;45(12):4058-4060.
110. Gallimore CI, Cubitt D, du Plessis N, Gray JJ. Asymptomatic and symptomatic excretion of noroviruses during a hospital outbreak of gastroenteritis. J Clin Microbiol. 2004;42(5):2271-2274.
111. Blanton LH, Adams SM, Beard RS, et al. Molecular and epidemiologic trends of caliciviruses associated with outbreaks of acute gastroenteritis in the United States, 2000-2004. J Infect Dis. 2006;193(3):413-421.
112. Mattison K, Karthikeyan K, Abebe M, et al. Survival of calicivirus in foods and on surfaces: experiments with feline calicivirus as a surrogate for norovirus. J Food Prot. 2007;70(2):500-503.
113. Lindesmith L, Moe C, Lependu J, Frelinger JA, Treanor J, Baric RS. Cellular and humoral immunity following Snow Mountain virus challenge. J Virol. 2005;79(5):2900-2909.
114. Fretz R, Herrmann L, Christen A, et al. Frequency of Norovirus in stool samples from patients with gastrointestinal symptoms in Switzerland. Eur J Clin Microbiol Infect Dis. 2005;24(3):214-216.
115. Fretz R, Svoboda P, Luthi TM, Tanner M, Baumgartner A. Outbreaks of gastroenteritis due to infections with Norovirus in Switzerland, 2001-2003. Epidemiol Infect. 2005;133(3):429-437.
116. Turcios RM, Widdowson MA, Sulka AC, Mead PS, Glass RI. Reevaluation of epidemiological criteria for identifying outbreaks of acute gastroenteritis due to norovirus: United States, 1998-2000. Clin Infect Dis. 2006;42(7):964-969.
117. Duizer E, Pielaat A, Vennema H, Kroneman A, Koopmans M. Probabilities in norovirus outbreak diagnosis. J Clin Virol. 2007;40(1):38-42.
118. Gray JJ, Kohli E, Ruggeri FM, et al. European multicenter evaluation of commercial enzyme immunoassays for detecting norovirus antigen in fecal samples. Clin Vaccine Immunol. 2007;14(10):1349-1355.
119. Richards AF, Lopman B, Gunn A, et al. Evaluation of a commercial ELISA for detecting Norwalk-like virus antigen in faeces. J Clin Virol. 2003;26(1):109-115.
120. Khamrin P, Nguyen TA, Phan TG, et al. Evaluation of immunochromatography and commercial enzyme-linked immunosorbent assay for rapid detection of norovirus antigen in stool samples. J Virol Methods. 2008;147(2):360-363.
121. Wiechers C, Bissinger AL, Hamprecht K, Kimmig P, Jahn G, Poets CF. Apparently non-specific results found using a norovirus antigen immunoassay for fecal specimens from neonates. Journal of Perinatology. 2008;28(1):79-81.
122. Castriciano S, Luinstra K, Petrich A, et al. Comparison of the RIDASCREEN norovirus enzyme immunoassay to IDEIA NLV GI/GII by testing stools also assayed by RT-PCR and electron microscopy. J Virol Methods. 2007;141(2):216-219.
123. Wilhelmi de Cal I, Revilla A, del Alamo JM, Roman E, Moreno S, Sanchez-Fauquier A. Evaluation of two commercial enzyme immunoassays for the detection of norovirus in faecal samples from hospitalised children with sporadic acute gastroenteritis. Clin Microbiol Infect. 2007;13(3):341-343.
124. de Bruin E, Duizer E, Vennema H, Koopmans MP. Diagnosis of Norovirus outbreaks by commercial ELISA or RT-PCR. J Virol Methods. 2006;137(2):259-264.
125. Okitsu-Negishi S, Okame M, Shimizu Y, et al. Detection of norovirus antigens from recombinant virus-like particles and stool samples by a commercial norovirus enzyme-linked immunosorbent assay kit. J Clin Microbiol. 2006;44(10):3784-3786.

126. Burton-MacLeod JA, Kane EM, Beard RS, Hadley LA, Glass RI, Ando T. Evaluation and comparison of two commercial enzyme-linked immunosorbent assay kits for detection of antigenically diverse human noroviruses in stool samples. J Clin Microbiol. 2004;42(6):2587-2595.
127. Christen A, Fretz R, Tanner M, Svoboda P. Evaluation of a commercial ELISA kit for the detection of Norovirus antigens in human stool specimens. Mitteilungen aus Lebensmitteluntersuchung und Hygiene.Bundesamt fur Gesundheit. 2003;94(6):594-602.
128. Gunson RN, Miller J, Carman WF. Comparison of real-time PCR and EIA for the detection of outbreaks of acute gastroenteritis caused by norovirus. Commun Dis Public Health. 2003;6(4):297-299.
129. Nordgren J, Bucardo F, Dienus O, Svensson L, Lindgren PE. Novel light-upon-extension real-time PCR assays for detection and quantification of genogroup I and II noroviruses in clinical specimens. J Clin Microbiol. 2008;46(1):164-170.
130. De Medici D, Suffredini E, Crudeli S, Ruggeri FM. Effectiveness of an RT-booster-PCR method for detection of noroviruses in stools collected after an outbreak of gastroenteritis. J Virol Methods. 2007;144(1-2):161-164.
131. Hymas W, Atkinson A, Stevenson J, Hillyard D. Use of modified oligonucleotides to compensate for sequence polymorphisms in the real-time detection of norovirus. J Virol Methods. 2007;142(1-2):10-14.
132. Logan C, O'Leary JJ, O'Sullivan N. Real-time reverse transcription PCR detection of norovirus, sapovirus and astrovirus as causative agents of acute viral gastroenteritis. J Virol Methods. 2007;146(1-2):36-44.
133. Menton JF, Kearney K, Morgan JG. Development of a real-time RT-PCR and Reverse Line probe Hybridisation assay for the routine detection and genotyping of Noroviruses in Ireland. Virol J. 2007;4:86.
134. Wolf S, Williamson WM, Hewitt J, et al. Sensitive multiplex real-time reverse transcription-PCR assay for the detection of human and animal noroviruses in clinical and environmental samples. Appl Environ Microbiol. 2007;73(17):5464-5470.
135. Yoda T, Suzuki Y, Yamazaki K, et al. Evaluation and application of reverse transcription loop-mediated isothermal amplification for detection of noroviruses. J Med Virol. 2007;79(3):326-334.
136. Antonishyn NA, Crozier NA, McDonald RR, Levett PN, Horsman GB. Rapid detection of Norovirus based on an automated extraction protocol and a real-time multiplexed single-step RT-PCR. J Clin Virol. 2006;37(3):156-161.
137. Hohne M, Schreier E. Detection and Characterization of Norovirus Outbreaks in Germany: Application of a One-Tube RT-PCR Using a Fluorogenic Real-Time Detection System. J Med Virol. 2004;72(2):312-319.
138. Rohayem J, Berger S, Juretzek T, et al. A simple and rapid single-step multiplex RT-PCR to detect Norovirus, Astrovirus and Adenovirus in clinical stool samples. J Virol Methods. 2004;118(1):49-59.
139. Schmid M, Oehme R, Schalasta G, Brockmann S, Kimmig P, Enders G. Fast detection of Noroviruses using a real-time PCR assay and automated sample preparation. BMC Infect Dis. 2004;4:15.
140. Vinje J, Vennema H, Maunula L, et al. International collaborative study to compare reverse transcriptase PCR assays for detection and genotyping of noroviruses. J Clin Microbiol. 2003;41(4):1423-1433.
141. Tatsumi M, Nakata S, Sakai Y, Honma S, Numata-Kinoshita K, Chiba S. Detection and differentiation of Norwalk virus by reverse transcription-polymerase chain reaction and enzyme-linked immunosorbent assay. J Med Virol. 2002;68(2):285-290.
142. O'Neill HJ, McCaughey C, Wyatt DE, Mitchell F, Coyle PV. Gastroenteritis outbreaks associated with Norwalk-like viruses and their investigation by nested RT-PCR. BMC Microbiol. 2001;1:14.
143. Jean J, D'Souza D, Jaykus LA. Transcriptional enhancement of RT-PCR for rapid and sensitive detection of Noroviruses. FEMS Microbiol Lett. 2003;226(2):339-345.

144. Greene SR, Moe CL, Jaykus LA, Cronin M, Grosso L, Aarle P. Evaluation of the NucliSens Basic Kit assay for detection of Norwalk virus RNA in stool specimens. J Virol Methods. 2003;108(1):123-131.
145. Tian P, Mandrell R. Detection of norovirus capsid proteins in faecal and food samples by a real time immuno-PCR method. Journal of Applied Microbiology. 2006;100(3):564-574.
146. Beuret C. A simple method for isolation of enteric viruses (noroviruses and enteroviruses) in water. J Virol Methods. 2003;107(1):1-8.
147. Vinje J, Hamidjaja RA, Sobsey MD. Development and application of a capsid VP1 (region D) based reverse transcription PCR assay for genotyping of genogroup I and II noroviruses. J Virol Methods. 2004;116(2):109-117.
148. Murata T, Katsushima N, Mizuta K, Muraki Y, Hongo S, Matsuzaki Y. Prolonged norovirus shedding in infants <or=6 months of age with gastroenteritis. Pediatr Infect Dis J. 2007;26(1):46-49.
149. Rockx B, De Wit M, Vennema H, et al. Natural history of human calicivirus infection: a prospective cohort study. Clin Infect Dis. 2002;35(3):246-253.
150. Marshall JA, Salamone S, Yuen L, Catton MG, Wright JP. High level excretion of Norwalk-like virus following resolution of clinical illness. Pathology. 2001;33(1):50-52.
151. Hedlund K-, Bennet R, Eriksson M, Ehrnst A. Norwalk-like virus as a cause of diarrhea in a pediatric hospital. Clinical Microbiology and Infection. 1998;4(8):417-421.
152. Chiba S, Sakuma Y, Kogasaka R, et al. Fecal shedding of virus in relation to the days of illness in infantile gastroenteritis due to calicivirus. J Infect Dis. 1980;142(2):247-249.
153. Dalling J. A review of environmental contamination during outbreaks of Norwalk-like virus. Br J Infect Control. 2004;5(2):9-13.
154. Wu HM, Fornek M, Schwab KJ, et al. A norovirus outbreak at a long-term-care facility: the role of environmental surface contamination. Infect Control Hosp Epidemiol. 2005;26(10):802-810.
155. Jones EL, Kramer A, Gaither M, Gerba CP. Role of fomite contamination during an outbreak of norovirus on houseboats. Int J Environ Health Res. 2007;17(2):123-131.
156. Clay S, Maherchandani S, Malik YS, Goyal SM. Survival on uncommon fomites of feline calicivirus, a surrogate of noroviruses. Am J Infect Control. 2006;34(1):41-43.
157. Gallimore CI, Taylor C, Gennery AR, et al. Environmental monitoring for gastroenteric viruses in a pediatric primary immunodeficiency unit. J Clin Microbiol. 2006;44(2):395-399.
158. Kuusi M, Nuorti JP, Maunula L, et al. A prolonged outbreak of Norwalk-like calicivirus (NLV) gastroenteritis in a rehabilitation centre due to environmental contamination. Epidemiol Infect. 2002;129(1):133-138.
159. Cheesbrough JS, Green J, Gallimore CI, Wright PA, Brown DW. Widespread environmental contamination with Norwalk-like viruses (NLV) detected in a prolonged hotel outbreak of gastroenteritis. Epidemiol Infect. 2000;125(1):93-98.
160. Schvoerer E, Bonnet F, Dubois V, et al. A hospital outbreak of gastroenteritis possibly related to the contamination of tap water by a small round structured virus. J Hosp Infect. 1999;43(2):149-154.
161. Green J, Wright PA, Gallimore CI, Mitchell O, Morgan-Capner P, Brown DW. The role of environmental contamination with small round structured viruses in a hospital outbreak investigated by reverse-transcriptase polymerase chain reaction assay. J Hosp Infect. 1998;39(1):39-45.

162. D'Souza DH, Sair A, Williams K, et al. Persistence of caliciviruses on environmental surfaces and their transfer to food. Int J Food Microbiol. 2006;108(1):84-91.
163. Paulson DS. The transmission of surrogate Norwalk virus - from inanimate surfaces to gloved hands: is it a threat? Food Protection Trends.International Association for Food Protection. 2005;25(6):450-454.
164. Lopman BA, Reacher MH, Vipond IB, et al. Epidemiology and cost of nosocomial gastroenteritis, Avon, England, 2002-2003. Emerg Infect Dis. 2004;10(10):1827-1834.
165. Billgren M, Christenson B, Hedlund KO, Vinje J. Epidemiology of Norwalk-like human caliciviruses in hospital outbreaks of acute gastroenteritis in the Stockholm area in 1996. J Infect. 2002;44(1):26-32.
166. Hansen S, Stamm-Balderjahn S, Zuschneid I, et al. Closure of medical departments during nosocomial outbreaks: data from a systematic analysis of the literature. J Hosp Infect. 2007;65(4):348-353.
167. Zingg W, Colombo C, Jucker T, Bossart W, Ruef C. Impact of an outbreak of norovirus infection on hospital resources. Infect Control Hosp Epidemiol. 2005;26(3):263-267.
168. Johnston CP, Qiu H, Ticehurst JR, et al. Outbreak management and implications of a nosocomial norovirus outbreak. Clin Infect Dis. 2007;45(5):534-540.
169. Leuenberger S, Widdowson MA, Feilchenfeldt J, Egger R, Streuli RA. Norovirus outbreak in a district general hospital--new strain identified. Swiss Med Wkly. 2007;137(3-4):57-81.
170. Cheng FW, Leung TF, Lai RW, Chan PK, Hon EK, Ng PC. Rapid control of norovirus gastroenteritis outbreak in an acute paediatric ward. Acta Paediatr. 2006;95(5):581-586.
171. Simon A, Schildgen O, Maria Eis-Hubinger A, et al. Norovirus outbreak in a pediatric oncology unit. Scand J Gastroenterol. 2006;41(6):693-699.
172. Conway R, Bunt S, Mathias E, Said H. The Norovirus experience: an exercise in outbreak management at a tertiary referral hospital. Aust Infect Control. 2005;10(3):95, 97-102.
173. Cooper E, Blamey S. A nopwvmus gastroenter-itis epidemic in a long-term-carefacility. Infection Control and Hospital Epidemiology. 2005;26(3):256-258.
174. Navarro G, Sala RM, Segura F, et al. An outbreak of norovirus infection in a long-term-care unit in Spain. Infect Control Hosp Epidemiol. 2005;26(3):259-262.
175. Schmid D, Lederer I, Pichler AM, Berghold C, Schreier E, Allerberger F. An outbreak of Norovirus infection affecting an Austrian nursing home and a hospital. Wien Klin Wochenschr. 2005;117(23-24):802-808.
176. Weber DJ, Sickbert-Bennett EE, Vinje J, et al. Lessons learned from a norovirus outbreak in a locked pediatric inpatient psychiatric unit. Infect Control Hosp Epidemiol. 2005;26(10):841-843.
177. Lynn S, Toop J, Hanger C, Millar N. Norovirus outbreaks in a hospital setting: the role of infection control. N Z Med J. 2004;117(1189):U771.
178. Khanna N, Goldenberger D, Graber P, Battegay M, Widmer AF. Gastroenteritis outbreak with norovirus in a Swiss university hospital with a newly identified virus strain. J Hosp Infect. 2003;55(2):131-136.
179. McCall J, Smithson R. Rapid response and strict control measures can contain a hospital outbreak of Norwalk-like virus. Commun Dis Public Health. 2002;5(3):243-246.

180. Milazzo A, Tribe IG, Ratcliff R, Doherty C, Higgins G, Givney R. A large, prolonged outbreak of human calicivirus infection linked to an aged-care facility. Commun Dis Intell. 2002;26(2):261-264.
181. Miller M, Carter L, Scott K, Millard G, Lynch B, Guest C. Norwalk-like virus outbreak in Canberra: implications for infection control in aged care facilities. Commun Dis Intell. 2002;26(4):555-561.
182. Hoyle J. Managing the challenge of an acute gastroenteritis outbreak caused by a Norwalk-like virus in a 239 bed long-term care facility. Aust Infect Control. 2001;6(4):128-133.
183. Russo PL, Spelman DW, Harrington GA, et al. Concise communications. Hospital outbreak of Norwalk-like virus. Infect Control Hosp Epidemiol. 1997;18(8):576-579.
184. Stevenson P, McCann R, Duthie R, Glew E, Ganguli L. A hospital outbreak due to Norwalk virus. J Hosp Infect. 1994;26(4):261-272.
185. Hudson JB, Sharma M, Petric M. Inactivation of Norovirus by ozone gas in conditions relevant to healthcare. J Hosp Infect. 2007;66(1):40-45.
186. Park GW, Boston DM, Kase JA, Sampson MN, Sobsey MD. Evaluation of liquid- and fog-based application of Sterilox hypochlorous acid solution for surface inactivation of human norovirus. Appl Environ Microbiol. 2007;73(14):4463-4468.
187. Poschetto LF, Ike A, Papp T, Mohn U, Bohm R, Marschang RE. Comparison of the sensitivities of noroviruses and feline calicivirus to chemical disinfection under field-like conditions. Appl Environ Microbiol. 2007;73(17):5494-5500.
188. Jimenez L, Chiang M. Virucidal activity of a quaternary ammonium compound disinfectant against feline calicivirus: a surrogate for norovirus. Am J Infect Control. 2006;34(5):269-273.
189. Kramer A, Galabov AS, Sattar SA, et al. Virucidal activity of a new hand disinfectant with reduced ethanol content: comparison with other alcohol-based formulations. J Hosp Infect. 2006;62(1):98-106.
190. Malik YS, Allwood PB, Hedberg CW, Goyal SM. Disinfection of fabrics and carpets artificially contaminated with calicivirus: relevance in institutional and healthcare centres. J Hosp Infect. 2006;63(2):205-210.
191. Malik YS, Maherchandani S, Goyal SM. Comparative efficacy of ethanol and isopropanol against feline calicivirus, a norovirus surrogate. Am J Infect Control. 2006;34(1):31-35.
192. Malik YS, Goyal SM. Virucidal efficacy of sodium bicarbonate on a food contact surface against feline calicivirus, a norovirus surrogate. International Journal of Food Microbiology. 2006;109(1/2):160-163.
193. Kampf G, Grotheer D, Steinmann J. Efficacy of three ethanol-based hand rubs against feline calicivirus, a surrogate virus for norovirus. J Hosp Infect. 2005;60(2):144-149.
194. Barker J, Vipond IB, Bloomfield SF. Effects of cleaning and disinfection in reducing the spread of Norovirus contamination via environmental surfaces. J Hosp Infect. 2004;58(1):42-49.
195. Duizer E, Bijkerk P, Rockx B, De Groot A, Twisk F, Koopmans M. Inactivation of caliciviruses. Appl Environ Microbiol. 2004;70(8):4538-4543.
196. Gehrke C, Steinmann J, Goroncy-Bermes P. Inactivation of feline calicivirus, a surrogate of norovirus (formerly Norwalk-like viruses), by different types of alcohol in vitro and in vivo. J Hosp Infect. 2004;56(1):49-55.
197. Lin CM, Wu FM, Kim HK, Doyle MP, Michael BS, Williams LK. A comparison of hand washing techniques to remove Escherichia coli and caliciviruses under natural or artificial fingernails. J Food Prot. 2003;66(12):2296-2301.

198. Nuanualsuwan S, Mariam T, Himathongkham S, Cliver DO. Ultraviolet inactivation of feline calicivirus, human enteric viruses and coliphages. Photochemistry and Photobiology. 2002;76(4):406-410.
199. Gulati BR, Allwood PB, Hedberg CW, Goyal SM. Efficacy of commonly used disinfectants for the inactivation of calicivirus on strawberry, lettuce, and a food-contact surface. J Food Prot. 2001;64(9):1430-1434.
200. Doultree JC, Druce JD, Birch CJ, Bowden DS, Marshall JA. Inactivation of feline calicivirus, a Norwalk virus surrogate. J Hosp Infect. 1999;41(1):51-57.
201. Shin GA, Sobsey MD. Reduction of norwalk virus, poliovirus 1 and coliphage MS2 by monochloramine disinfection of water. Water Science and Technology. 1998;38(12):151-154.
202. Rossignol JF, El-Gohary YM. Nitazoxanide in the treatment of viral gastroenteritis: a randomized double-blind placebo-controlled clinical trial. Aliment Pharmacol Ther. 2006;24(10):1423-1430.
203. Gustafson TL, Kobylik B, Hutcheson RH, Schaffner W. Protective effect of anticholinergic drugs and psyllium in a nosocomial outbreak of Norwalk gastroenteritis. J Hosp Infect. 1983;4(4):367-374.
204. Yoder J. Roberts V. Craun GF. Hill V. Hicks LA. Alexander NT. Radke V. Calderon RL. Hlavsa MC. Beach MJ. Roy SL. Centers for Disease Control and Prevention (CDC). Surveillance for waterborne disease and outbreaks associated with drinking water and water not intended for drinking--United States, 2005-2006. Morb Mortal Wkly Rep Surveill Summ. 2008;57(9):39-62.
205. Cooper E, Blamey S. A norovirus gastroenteritis epidemic in a long-term-care facility. Infect Control Hosp Epidemiol. 2005;26(3):256-258.
206. Russo PL, Spelman DW, Harrington GA, et al. Hospital outbreak of Norwalk-like virus. Infect Control Hosp Epidemiol. 1997;18(8):576-579.
207. Centers for Disease Control and Prevention (CDC). Multisite outbreak of norovirus associated with a franchise restaurant--Kent County, Michigan, May 2005. MMWR. 2006;55(14):395-397.